American Journal of Diseases of Children

VOL. 1 MAY, 1911 No. 5

STUDIES ON INFANT NUTRITION

UNDER THE DIRECTION OF L. EMMETT HOLT, M.D., AND P. A. LEVENE, M.D.

I. Metabolism in Chronic Malnutrition *

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Growth is the principal function of infancy, and any disturbance of it constitutes a serious condition. A state of nutrition which maintains the weight and size of the organism unchanged is desirable for the adult; it cannot be endured with impunity for any length of time by the infant.

Unfortunately disturbances of nutrition are not infrequent, principally among artificially-fed infants. The condition may follow some acute disease or may develop gradually as a result of some form of irrational feeding. It has been named differently by various writers at different times. It has been studied as atrophy, marasmus, simple wasting, decomposition, etc. But, notwithstanding the numerous investigations into its nature, and notwithstanding the many theories advanced for the explanation of the condition, the actual pathogenesis of the retarded growth of these infants still remains obscure.

In view of these considerations an attempt has been made to study the metabolism of infants in different phases of this condition. The difficulties of the undertaking were fully realized. In addition to those that are common to all metabolism work, there are additional factors arising from the technic of the investigation on infants. The position and restraint necessary in the metabolism apparatus, and even the surroundings of the hospital, affect the general health of an infant much more than the usual routine of a metabolism experiment affects the adult.

However, it was hoped that a careful study of a considerable number of patients, extended over a long period of time, would furnish information which might serve to establish a rational treatment of these disturbances. The patients on whom these studies have been made were all inmates of the Babies' Hospital, and for the most part they were admitted for disordered nutrition. The clinical details have been carried

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The present communication may be regarded as preliminary and contains a report on metabolism experiments on seven infants. The age of the patients varied from 3 to 7 months, and the duration of the observation from 3 to 106 days. The last represents the longest metabolism experiment on an infant thus far recorded. Attention has been paid to the nitrogen metabolism, fat metabolism, and to a certain extent to the mineral and water balance.

The food analysis was made in every experiment.

METHODS OF ANALYSIS

Total nitrogen in food mixture, urine, and dried feces was determined by the Kjeldahl-Gunning method.

Ammonia nitrogen was determined by the Folin method.

Sugar was determined by Pavy's method.

Starch when present was first hydrolyzed by heating with dilute sulphuric acid in an autoclave, and the sugar thus formed titrated according to Pavy.

Fat estimation: In order to determine the total fatty acids, food mixtures or feces were evaporated to dryness on a water-bath. Samples of the dry residues were thoroughly mixed with dilute phosphoric acid and the mixtures extracted in a Soxhlet apparatus with ether. In order to free the ethereal residues from moisture they were redissolved in chloroform, filtered through filter paper saturated with chloroform, and the weight of the chloroform residue determined. The neutral fat and free fatty acids were determined by extracting the dry samples of food-mixtures or feces with ether.

The total ash was obtained by igniting the dried feces and the residues from the evaporated urine with a few drops of concentrated nitric and sulphuric acid. The bases were calculated as sulphates.

Phosphoric acid was determined by titration with uranium acetate. For determination of phosphoric acid in the feces, the ash was dissolved in the smallest possible quantity of concentrated hydrochloric acid. An aliquot part of the solution was neutralized with sodium acetate and titrated with uranium acetate.

Calcium estimation was carried out in the usual manner. It was precipitated from solution by means of ammonium oxalate. The oxalate was transformed by ignition into the oxid. The calcium content of the urine was found too small to make possible an accurate determination.

The clinical histories of the patients are given at the end of the report. The results of the analyses are tabulated (Tables 1, 2 and 3).

The discussion of the results will be directed principally to the analysis of the peculiarities of nitrogen and fat metabolism. Carbohydrate, mineral and water balance will be discussed only in their effect on either protein or fat assimilation.

NITROGEN METABOLISM

A. General Considerations

Protein was regarded for a long time as the exclusive foodstuff on which depended the growth of the young. The utility of a foodstuff according to the views of those days, was determined principally by the digestibility of its protein material. These views, however, collapsed as soon as they were subjected to the experimental test. Rubner and Heubner have made it clear that fat and carbohydrates share equally with protein in their power to aid the maintenance and growth of the young as they do in maintaining the integrity of the adult. The law of the isodynamic value of these three principal sources of animal energy is applicable to all ages. Later investigations have demonstrated that in health practically every protein is equally well digested and absorbed from the intestinal tract of the infant; and further, it was established that in health, fat has an insignificant influence on the rate of absorption and assimilation of protein, while the influence in this direction of carbohydrate is very marked, exercising a protecting power over the combustion of protein and therefore increasing the degree of its assimilation.

Notwithstanding the revision in the view of the rôle of protein in the process of nutrition of the infant, it remains true that growth of tissues cannot take place without a retention of nitrogen in the organism. It is natural to find, therefore, that considerable attention was devoted to the study of nitrogen metabolism in conditions of malnutrition.

The earlier investigations into the nitrogen metabolism of atrophic children belong to Rubner and Heubner,[1] to Baginsky,[2] and to Bendix.[3] In the patients of Rubner and Heubner and of Baginsky, protein assimilation was lowered. Baginsky reached the conclusion that infantile atrophy was caused by disturbed assimilation resulting from the atrophic changes in the gastro-intestinal tract.[4] Also in the patient of Heubner and Rubner the absorption was apparently defective. Bendix was the first to make the observation that normal protein metabolism coexisted

1. Rubner and Heubner: Ztschr. f. Biol., 1899, xxxviii, 360.
2. Baginsky: Deutsch. med. Wchnschr., 1899, xviii, 281.
3. Bendix: Arch. f. Anat. u. Physiol. Suppl. Vol., 1899, 206.
4. In this discussion the term "atrophic" will be abandoned, and the terms of Finkelstein—decomposition and intoxication—will not be made use of. All the various conditions that result in the retardation or the apparently complete arrest of growth will be referred to as infantile malnutrition.

TABLE 1.—Average Daily Food Intake and Weight Balance

Period	Dates	Composition of Food	Volume of Milk c.c.	Protein Gms.	Carbohydrate Gms.	Fat Gms.	Weight Balance* Gms.
		I. JANES					
1	Nov. 18-22	½ milk, 5% lime-water, barley-water to volume, 3¾% milk-sugar additional	512	18.0	30.8	23.3	+36.8
2	Nov. 23-26	Same, except 5 5/7% milk-sugar	525	18.1	66.2	18.1	+46.0
3	Nov. 28-Dec. 1	50-60% skimmed-milk, 5% lime-water, barley-water to volume, 5% milk-sugar	578	19.4	51.4	10.7	—10.6
4	Dec. 8-16	55-65% skimmed-milk, 5% lime-water, concentrated barley-water to volume	651	25.0	39.3	14.9	+ 9.4
5	Dec. 18-20	65% skimmed-milk, 5% lime-water, conc. barley-water to vol., 12 c.c. Mellin's Food	651	24.0	54.3	18.3	+14.2
6	Dec. 22-24	Same, except no Mellin's Food	651	25.8	39.4	15.8	+18.9
7	Dec. 31-Jan. 3	⅔ milk, 5% lime-water, water to volume	770	27.3	31.4	31.5	+60.2
8	Jan. 5-6	Same, but peptonized	770	26.0	29.7	27.0	—42.5
9	Jan. 9-14	¾ skimmed-milk, ¼ water, 3.08 gms. $NaHCO_3$	880	28.0	33.7	12.1	+ 2.4
10	Jan. 22-24	½ skimmed-milk (3 oz. off top), ½ soy bean gruel, 2 gms. NaCl, 16 c.c. beef-juice	604	26.1	26.0	16.2	+55.6
11	Jan. 26-28	Same, except milk 4 oz. off top	604	26.3	27.6	7.9	—54.0
12	Feb. 19-24	½ fat-free milk, ½ soy bean gruel, 2 gms. NaCl, 32 c.c. beef-juice, 1.2% olive oil	508	24.9	23.0	14.2	—25.8
13	Feb. 25-Mar. 2	Same, except 1.6-2.0% olive oil	525	27.2	25.9	18.8	+ 5.2
		II. DAKAK					
1	Mar. 8-11	Skimmed-milk, 5% lime-water, milk-sugar to 6%, 20 c.c. malt soup extract	1050	18.1	67.9	19.7	+48.5
2	Mar. 12-14	Same, except only 12 c.c. malt soup extract	641	10.8	38.2	12.3	+ 4.3
		III. STOCKER					
1	Mar. 17-18	40% milk, 5% lime-water, barley-water to volume, 4 1/6% milk-sugar additional	415	15.2	60.4	17.0	+68.5
2	Mar. 19-20	Same, except milk-sugar only to 3%	418	15.3	38.2	18.7	+ 7.7

3	Mar. 23-24	Same, except no additional milk-sugar	462	16.6	29.2	22.4	—10.0
4	Mar. 26-27	Same, except 10 c.c. malted milk additional	462	16.1	32.9	16.3	+72.5
5	Mar. 28	Same as in Period 3	462	14.4	29.2	19.9	— 7.0
6	Mar. 29	40% milk, 5% lime-water, arrow-root gruel (2 drams to pt.) to volume	462	13.8	26.8	15.5	—12.0
7	Mar. 31-Apr. 1	35% fat-free milk, 5% lime-water, soy bean gruel (1 oz. to pt.) to volume	404	17.9	19.5	2.3	—80.5
		IV. GUERIN					
1	Apr. 13-16	45% milk, 5% lime-water, barley-water to vol., 2 13/16% milk-sugar additional, 16 c.c. malt soup ext., albumin of 2 eggs	473	25.5	50.3	17.9	+ 8.5
2	Apr. 18-25	Same, except 50% milk	479	27.0	51.5	22.5	+23.4
3	Apr. 27-29	Same with 6 c.c. olive-oil	479	26.9	49.1	29.8	—17.0
4	May 1-2	40% milk, 5% lime-water, barley-water to vol., 16 c.c. malt soup ext., albumin of 2 eggs, 8 c.c. olive-oil	120	23.5	47.7	25.5	— 1.0
		V. FRANCO					
1	May 7-10	40% milk, 5% lime-water, barley-water to volume, milk-sugar to 5%, 12 c.c. malt soup extract	414	16.0	60.6	15.8	+27.8
2	May 22-27	Same, with 4 gms. NaCl	420	15.5	55.0	14.0	+ 4.6
3	May 28-30	Same, except 5 gms. NaCl	417	15.7	54.1	12.9	+ 1.7
		VI. VOGELIN					
1	May 13-15	45% milk, 5% lime-water, barley-water to volume, milk-sugar to 5%, 12 c.c. malt-soup extract	473	18.2	56.3	15.0	—25.0
		VII. DOLAN					
1	May 18-20	40% milk, 5% lime-water, barley-water to volume, milk-sugar	420	16.3	57.1	21.8	—18.7
	May 18-19	to 5%, 20 c.c. malt soup extract, 6 c.c. olive-oil	420	16.8	57.1	22.3	—14.5
	May 20		420	15.1	57.1	20.8	—27.0

*By weight balance is meant average gain or loss per twenty-four hours.

with the condition of chronic malnutrition. Later similar observations were recorded by many writers[5] on protein metabolism in infants.

B. Protein Absorption

Protein absorption generally is measured by the difference in the values of the nitrogen intake and of the nitrogen content of the feces. However, in recent years attention has been called by Orgler[6] to the fact that the nitrogenous portion of the feces is composed not exclusively of the unabsorbed residue of the food nitrogen, but contains the nitrogenous substances of the intestinal secretions. Orgler, in fact, regards all the nitrogen of the feces as derived from the latter source. So long, however, as the source of the feces nitrogen is not as yet fully established, it was considered more conservative to estimate the value of protein absorption by the old method, bearing in mind that the values obtained in this manner are minimal.

It has been pointed out by Orgler that the nitrogen output through feces remains approximately constant, regardless of the nitrogen intake, although the value varies for every infant. The observations on our patients (Table 2) harmonize with this view. Thus, in Janes (Case 1) the nitrogen content of the feces was for only one day 0.23 gm. and for two days about 0.35 gm. each day. In the other periods, the output was about 0.40 gm. and only once reached 0.78 gm. Thus the value was not absolutely constant, though the fluctuations were not very great. It remained practically constant when there was little variation in the nitrogen intake. Thus in the three experiments on Franco (Case 5) the intake remained 2.56, 2.47, 2.51 gm. nitrogen per day of each period, and the nitrogen output for each of the three periods was 0.49, 0.48, 0.50 gm. The proportion of absorbed nitrogen varied in Janes (Case 1) from 80 to 91.5 per cent., the average being about 87.0 per cent. of the intake. In all other patients the absorption exceeded considerably 80 per cent. of the intake, with the exception only of Stocker (Case 3). In this instance the low average of nitrogen absorption of about 78 per cent. was conditioned by higher intestinal peristalsis. Thus, from the standpoint of protein absorption our patients presented little abnormality.

C. Nitrogen Balance

The nitrogen retention reached a higher value in those of our patients who showed a very considerable gain in weight in course of the experi-

5. Orgler: Jahrb. f. Kinderh., 1908, lxvii, 383; Monatschr. f. Kinderh., 1908, 135; Freund: Jahrb. f. Kinderh., 1904, lix, 421; 1905, lxi, 36; Cronheim and Muller: Biochem. Ztschr., 1908, ix, 76; Lange and Behrend: Jahrb. f. Kinderh., 1897, xliv, 337; Philips: Monatschr. f. Kinderh., 1906, 413; Meyer, L. F.: Jahrb. f. Kinderh., 1910, lxxi, 379.

6. Orgler: Ergebn. d. Inn. Med., 1908, ii, 464.

ment, and thus were in a state of reconvalescence. In Franco (Case 5), who was gaining weight continually, the nitrogen retention reached the high value of 41.8 per cent.; in Guerin (Case 4), who also showed a marked gain in weight during three experiments, the highest retention was 33.1 per cent. of the intake. On the other hand, in Janes (Case 1) no parallelism is noted between the curve indicating the gain in weight and that of nitrogen retention. Thus, during the period of the highest nitrogen retention of 1.091 gm. per day, the body weight showed no gain; and on the other hand in period 9, when the body weight reached the highest value of 4,680 gm., the nitrogen retention was only 0.552 gm. per day. However, most instructive is the consideration of the total nitrogen balance for the fifty-three days recorded in the tables. The total retention of nitrogen for the period was 34.53 gm. According to the analysis of W. Camerer,[7] Jr., the nitrogen content of a new-born infant is 1.95 per cent. On the basis of this the nitrogen gain ought to correspond to 1.726 gm. The ultimate gain in weight was only 120.0 gm. Admitting that the value of Camerer is not absolutely correct, and that some of our values are not free from error, one nevertheless is impressed by the fact that during the time of the experiment there was undoubtedly a considerable growth of the mass of cellular material, without any marked increase in the body weight. It must be mentioned in this connection that Camerer has also noted a gain in the size of infants without a corresponding gain in weight.

FAT METABOLISM

A. General Considerations

According to the view of the majority of writers, the most striking manifestation of abnormal metabolism in infantile malnutrition is the response of the organism to the administration of fat. Fat added to the food of normal infants in quantities exceeding considerably the average requirement does not alter in any way the character of the general metabolism, may not cause any disturbance, and on the contrary may bring about a rise in the rate of daily gain in weight.

In infantile malnutrition the response is very different. The most obvious abnormality and, from the practical standpoint, the most important one is, that the increase in the fat intake causes a disturbance of digestion and a loss instead of an increase in weight. The abnormal "weight response" is associated with symptoms of general discomfort. This peculiar influence of fat in infants with chronic malnutrition has been the subject of numerous experimental investigations. Steinitz,[8]

7. Camerer, W., Jr.: Ztschr. f. Biol., 1900, xxxix, 182; and Ztschr. f. Biol., 1900, xl, 531.
8. Steinitz: Jahrb. f. Kinderh., 1905, lvii, 689.

TABLE 2.—NITROGEN METABOLISM*

Period	Dates	Intake Total N., Gms.	Output: Urine Total N., Gms.	Urine Ammonia N., Gms.	Urine Ammonia N., Percent. Total N.	Output: Feces Total N., Gms.	Absorbed — Total N., Gms.	Absorbed — Percent. of Intake	Retained — Total N., Gms.	Retained — Percent. of Intake	Retained — Percent. of Absorbed
					I. JANES						
1	Nov. 18-22	2.88	2.01	.35	17.5†	.23	2.66	92.3	.64	22.3	24.1
2	Nov. 23-26	2.90	1.33	.52	38.6†	.57	2.33	80.4	.99	34.2	42.6
3	Nov. 28-Dec. 1	3.10	1.91	.71	37.0†	.53	2.58	83.2	.67	21.5	25.9
4	Dec. 8-16	4.00	2.94	.17	5.6	.35	3.66	91.4	.71	17.8	19.5
5	Dec. 18-20	3.84	2.79	.38	13.7†	.56	3.28	85.7	.49	12.7	14.9
6	Dec. 22-24	4.12	2.55	.18	6.9	.48	3.64	88.6	1.09	26.5	30.0
7	Dec. 31-Jan. 3	4.37	2.97	.23	7.8	.59	3.78	86.7	.80	18.4	21.3
8	Jan. 5-6	4.16	2.82	.15	5.4	.60	3.56	85.6	.74	17.8	20.8
9	Jan. 9-14	4.48	3.14	.09	2.8	.78	3.69	82.8	.55	12.3	14.9
10	Jan. 22-24	4.18	3.51	.12	3.4	.41	3.77	90.3	.26	6.3	7.0
11	Jan. 26-28	4.21	3.53	.10	2.9	.36	3.85	91.5	.32	7.6	8.3
12	Feb. 19-24	3.99	3.36	.18	5.2	.41	3.58	89.8	.22	5.6	6.2
13	Feb. 25-Mar. 2	4.35	2.95	.27	9.0	.51	3.85	88.4	.89	20.5	23.2
					II. DAKAK						
1	Mar. 8-11	2.89	1.55	.16	10.6	.54	2.35	81.5	.80	27.7	34.1
2	Mar 12-14	1.73	1.88	.13	7.1	.24	1.48	86.0	—.39	....	....
					III. STOCKER						
1	Mar. 17-18	2.43	.82	.26	32.0‡	.78	1.65	67.9	.83	34.1	50.3
2	Mar. 19-21	2.45	1.43	.31	21.9‡	.60	1.86	75.8	.43	17.6	23.2

3	Mar. 23-24	2.65	1.86	.34	18.2‡	.69	1.96	73.9	.10	3.7	5.0
4	Mar. 26-27	2.59	1.83	.36	19.9‡	.56	2.03	78.2	.20	7.7	9.9
5	Mar. 28	2.30	1.71	.32	18.9‡	.47	1.83	79.7	.13	5.4	6.8
6	Mar. 29	2.20	1.58	.33	20.7‡	.68	1.52	69.0	—.07	....	....
7	Mar. 31-Apr. 1	2.86	1.92	.30	15.6‡	.65	2.21	77.6	.29	10.3	13.2
	IV. GUERIN										
1	Apr. 13-16	4.08	2.22	.14	6.2	.68	3.40	83.5	1.18	29.1	34.8
2	Apr. 18-25	4.32	2.36	.15	6.3	.62	3.71	85.8	1.34	31.1	36.2
3	Apr. 27-29	4.31	2.11	.18	8.3	.77	3.53	82.2	1.43	33.1	40.3
4	May 1-2	3.76	2.12	.18	8.7	.68	3.08	81.8	.96	25.4	31.1
	V. FRANCO										
1	May 7-10	2.56	1.00	.09	9.3	.49	2.07	81.1	1.07	41.8	51.6
2	May 22-27	2.48	1.36	.11	7.9	.48	1.99	80.7	.63	25.5	31.7
3	May 28-30	2.51	1.52	.12	7.9	.50	2.01	80.2	.49	19.7	24.6
	VI. VOGELIN										
1	May 13-15	2.91	1.44	.16	11.2	.60	2.31	79.5	.86	29.7	37.4
	VII. DOLAN										
..	[May 18-19]..	2.69	1.59	.07	4.3	.31	2.29	88.2	.72	27.6	31.3
..	[May 20]....	2.41	1.56	.08	4.8	.26	2.43	90.3	.85	31.4	34.8
1	May 18-20	2.60	1.58	.07	4.4	.40	2.01	83 7	.46	18.9	22.6

*Figures represent average values for twenty-four hours.
†Urine alkaline.
‡Urine acid.

Keller,[9] Freund,[10] Birk,[11] Rothberg,[12] and L. F. Meyer[13] have furnished most valuable contributions in this connection. Special attention was paid by these authors to the mineral metabolism. But even after these recent contributions, the number of thoroughly described cases is not sufficient to permit establishing a clear causative relationship between the various symptoms observed in the course of this diseased condition. *A priori,* the ill effects of fat intake may be attributed to either one of the following assumptions:

1. Lack of absorption.

2. The effect of the fatty acids on the mineral metabolism. The presence in the intestinal wall of considerable quantities of soaps may lead to a deficient supply of mineral elements to the tissues.

B. Fat Absorption

In health comparatively little fat is removed by the feces, over 95 per cent. being absorbed from the intestinal tract. On this point most observers are in harmony. Less accord exists regarding the view on fat absorption in the various conditions of infantile malnutrition. According to Freund, even under abnormal conditions of nutrition, the fat absorption may remain perfectly normal, and he records instances in which with "soap stools" the fat absorption reached as high a value as 97 per cent. of the intake. On the other hand, Bahrdt,[14] Birk,[15] M. Chatruet,[16] Hecht,[17] and L. F. Meyer[13] record in conditions of malnutrition with "soap stools" a fall in the fat absorption averaging about 80 per cent.

In all patients under our observation the fat absorption was considerably below normal (Table 3). The lowest percentage noted in Janes (Case 1) was 52.3 per cent.; the highest, 95.8 per cent., the average varying between 70 and 80 per cent. The greatest loss of fat was undoubtedly caused by diarrhea, and the most complete absorption can be explained by the addition of olive-oil to the diet of that period. The other fluctuations were conditioned by the quantity of the fat intake. On the day of the highest intake 78.6 per cent. was absorbed. In the other patients the absorption fluctuated within the same limits, namely between 70 and 85 per cent. The only exception with a considerably lower fat absorption is presented by Stocker (Case 3), in whom the lowest rate of absorption fell to 34.2 per cent. and the highest did not reach above 71.5

9. Keller: Arch. f. Kinderh., 1900, xxix, 1.
10. Freund: Jahrb. f. Kinderh., 1905, lxi, 36.
11. Birk: Jahrb. f. Kinderh., 1907, lxvi, 300.
12. Rothberg: Jahrb. f. Kinderh., 1907, lxvi, 69.
13. Meyer, L. F.: Jahrb. f. Kinderh., 1910, lxxi, 379.
14. Bahrdt: Jahrb. f. Kinderh., 1910, lxxi, 249.
15. Birk: Jahrb. f. Kinderh., 1907, lxvi, 69.
16. Chatruet, M.: Thése de Paris, 1904.
17. Hecht: Jahrb. f. Kinderh., 1905, lxii, 613.

per cent. Again in this instance the low absorption was caused by increased peristalsis. On the other hand, the patient who showed the highest average fat absorption—Dolan (Case 7)—was receiving olive-oil. The beneficial effect of olive-oil on fat absorption had been noted already by Freund.[18]

According to his experiments the comparative degree of fat absorption on a diet containing no olive-oil, and one containing the oil (the total amount of fat intake being equal) varied as follows:

Cases	Diet	Per cent of Soap
A.	Meal	46.7
	Oil	7.9
	Malt	5.9
B.	Meal	57.0
	Oil	6.2
	Malt	5.0

In reviewing these observations on the fat absorption one is impressed by the fact that in all patients (with the exception of Dolan, Case 7), the loss of fat through the feces was not sufficient to cause in itself any perceptible deviation in the general nutrition.

C. Soap Content of the Feces

In health, according to Freund,[19] the average proportion of insoluble soaps in feces is 18.3 per cent. of the total fat in the feces, the lowest figure being 4.9 per cent. and the highest 35.9 per cent. In conditions of malnutrition the average reaches 48.0 per cent., the lowest being 42.1 per cent. and the highest 57.0 per cent.

In the patients under our observation the soap content of the feces varied considerably. The percentage of soap in the stools of Janes (Case 1) was as a rule very high, 83.5 per cent. in one period, and gave an average of 46.3 per cent. for the thirteen periods. The low content of soap of 11.0 per cent. was conditioned by diarrhea and on two other occasions the low percentage of soap in the feces was caused by the addition to the diet of olive-oil.

Of the other patients a high percentage of soap in the feces was noted only in Dakak (Case 2), the average being 66.7 per cent. and, as can be seen from the following table, the soap content of the remaining patients did not exceed the normal value.

Patients	Per cent. of Soap in Feces	Patients	Per cent. of Soap in Feces
Janes	46.3	Franco	11.66
Dakak	66.7	Vogelin	13.8
Stocker	20.3	Dolan	34.
Guerin	20.9		

18. Freund: Biochem. Ztschr., 1909, xvi, 453.
19. Freund: Ergebn. d. inn. Med., 1909, iii, 163.

TABLE 3.—Analysis of Fat and Ash

Period	Date	Fat					Water	Ash							
		Feces						Feces			Urine		Balance		
		Total Gms.	Neutral fat and Fatty Acids	Soap Gms.	Fat Percent. of Total	Percent. of Intake Absorbed	Feces c.c.	Total as Sulphates Gms.	Ca as Sulphates Gms.	P_2O_5 Gms.	Total as Sulphates Gms.	P_2O_5 Gms.	Approx. Intake as Oxids Gms.	Output as Oxids Gms.	Retained Oxids Gms.
		I. JANES													
1	Nov. 18-22	3.87	.82	3.05	78.9	83.4	29.8	2.94	2.69	.64	3.26	.47	4.07	2.63	1.44
2	Nov. 23-26	5.78	4.56	1.22	21.1	68.1	155.4	2.70	1.92	.60	2.64	.39	4.47	2.27	2.20
3	Nov. 28-Dec. 1	3.05	1.80	1.25	41.0	71.5	83.9	3.25	2.55	.73	3.98	.38	4.87	3.07	1.80
4	Dec. 8-16	2.28	.38	1.90	83.5	84.7	40.2	4.63	4.49	.68	3.92	.52	5.41	3.63	1.78
5	Dec. 18-20	4.01	2.00	2.01	50.2	78.1	74.6	4.40	2.12	1.12	3.79	.45	5.42	3.47	1.95
6	Dec. 22-24	3.35	1.33	2.02	60.3	78.8	109.8	3.98	2.88	.81	2.90	.53	5.42	2.92	2.50
7	Dec. 31-Jan. 3	6.75	3.42	3.33	49.3	78.6	64.8	4.38	3.74	1.16	2.16	.52	5.84	2.77	3.07
8	Jan. 5-6	7.57	4.49	3.08	40.8	72.0	89.8	4.67	3.83	.59	3.19	.48	5.84	3.33	2.51
9	Jan. 9-14	5.77	5.13	.64	11.1	52.3	139.0	5.15	3.35	.55	5.06	.43	7.74	4.33	3.41
10	Jan. 22-24	2.41	.71	1.70	70.6	85.1	56.1	5.21	3.82	1.48	4.16	.45	5.59	3.97	1.62
11	Jan. 26-28	1.69	.47	1.22	72.2	78.6	39.5	3.69	2.83	.48	4.24	.05	5.59	3.36	2.23
12	Feb. 19-24	.60	.54	.06	10.0	95.8	44.4	2.92	2.16	.74	4.63	.53	4.87	3.20	1.67
13	Feb. 25-Mar. 2	2.67	2.34	.33	12.4	85.8	131.5	3.93	2.24	1.12	3.49	.38	5.00	3.15	1.85
		II. DAKAK													
1	Mar. 8-11	6.04	2.73	3.31	54.8	69.2	68.9	3.46	....	.45	2.90	.59	7.93	2.70	5.23
2	Mar. 12-14	2.63	.56	2.07	78.7	78.6	23.0	1.70	....	.31	2.71	.18	4.84	1.87	2.97

	III. STOCKER														
1	Mar. 17-18	8.61	7.87	.74	8.6	49.4	355.0	4.03	....	.57	1.00	.06	3.64	2.13	1.51
2	Mar. 19-21	7.74	5.15	2.59	33.5	58.6	148.6	3.21	....	.82	1.63	.34	3.67	2.05	1.62
3	Mar. 23-24	8.11	5.98	2.13	26.3	63.9	246.2	4.15	....	.67	2.19	.23	4.01	2.69	1.32
4	Mar. 26-27	7.06	5.88	1.18	16.8	56.7	222.4	4.08	....	.67	2.17	.15	4.01	2.65	1.36
5	Mar. 28	5.67	3.83	1.84	32.5	71.5	239.2	3.56	....	....	2.19	...	4.01	2.44	1.57
6	Mar. 29	10.18	10.18	....	....	34.2	279.4	4.65	....	.60	2.84	.11	4.01	3.18	.83
7	Mar. 31-Apr. 1..	1.39	1.05	.34	24.5	40.0	225.8	3.56	....	.67	.71	.13	3.57	1.81	1.76
	IV. GUERIN														
1	Apr. 13-16	2.04	1.41	.63	30.8	88.6	71.7	2.05	....	.24	3.77	.17	4.07	2.47	1.60
2	Apr. 18-25	2.85	1.85	1.00	35.1	87.3	68.0	2.04	....	.23	3.06	.33	4.12	2.16	1.96
3	Apr. 27-29	4.32	3.27	1.05	24.3	85.5	80.7	2.51	....	.38	2.57	.12	4.12	2.15	1.97
4	May 1-2	6.10	5.03	1.07	17.6	76.1	80.3	2.00	....	.23	3.82	.15	3.68	2.47	1.21
	V. FRANCO														
1	May 7-10	3.07	2.62	.45	14.7	80.5	141.4	2.77	....	.30	2.65	.13	3.64	2.30	1.34
2	May 22-27	3.23	2.84	.39	12.1	76.8	129.6	2.69	....	.17	5.24	.12	5.80	3.36	2.44
3	May 28-30	2.95	2.69	.24	8.2	77.3	95.2	2.73	....	.23	6.99	.12	6.31	4.12	2.19
	VI. VOGELIN														
1	May 13-15	4.42	3.81	.61	13.8	70.6	160.2	2.95	....	.32	1.78	.26	4.08	2.01	2.07
	VII. DOLAN														
1	May 18-20	3.09	1.95	1.14	36.9	85.9	31.8	2.04	....	.26	2.54	.17	3.68	1.94	1.74
..	[May 18-19]	2.76	1.32	1.44	52.2	87.7	17.3	....	....	....	....	...	....	....	....
..	[May 20]	3.76	3.20	.56	14.9	81.9	60.9	....	....	....	....	...	....	....	....

The lowest percentage of soap was noted in Franco (Case 5), who at the time of the metabolism experiment was in a condition of reconvalescence. Vogelin (Case 6) also was in a condition of reconvalescence, gaining weight at the beginning of the experiment, although his condition became aggravated during the experiment. On the other hand, Dakak (Case 2) was apparently in a comparatively good condition, showing a gain in weight during the time of the metabolism experiment, and yet the percentage of soap in his feces was very high.

It must, however, be borne in mind that all other observations with the exception of the one on Janes (Case 1) were of comparatively short duration, and therefore are less instructive. But, even in the case of Janes, it is as yet difficult to determine the factors which control the soap formation. Comparing three periods, the fourth, fifth and sixth, which differ principally in the carbohydrate intake, one notes that the lowest percentage of soap formation coincides with the period of the highest carbohydrate intake. Also very instructive are the last three periods. They all differ principally in their fat intake. The highest content of soap in the feces coincides with the lowest fat intake. At first glance, the result seems very paradoxical. However, it is possible that the addition of olive-oil to the diet of the last two periods conditioned the improvement in the fat absorption and the fall in the ratio of soap formation.

Thus the analysis of the composition of the fat of the feces in infantile malnutrition leads to the conclusion that in this condition the fat absorption from the small intestines is diminished. The unabsorbed fat, fatty acid and alkaline soaps, therefore, reach the colon. There the fat, fatty acids and the alkaline soaps are transformed into insoluble calcium soaps.

D. Salt Content of the Feces

The abnormal soap formation may lead to a fundamental change in the character of the general composition of the feces, which in its turn may affect the general health and the growth of an infant. Thus, *a priori*, by the formation of calcium soaps, the insoluble phosphates may be transformed into soluble salts, and in this manner may suffer absorption. The theoretical considerations were corroborated by experiment. In healthy infants with a normal fat absorption, high fat intake remains without influence on the mineral composition of the feces. In chronic malnutrition the salt output through the feces is considerably raised by the fat of the diet. This was demonstrated by Steinitz,[8] Freund,[10] Rothberg,[12] Birk,[11] and L. F. Meyer.[13] Experimentally the same effect of high fat intake was observed by Schlesinger[19] on dogs after the removal of the pancreas. The loss of mineral bases after high fat intake may reach

19. Naunyn's Festschrift: Ztschr. f. klin. Med., 1904, lv, 214.

a degree sufficient to produce a negative salt balance, which alone may arrest further growth. This consideration perhaps more than anything else, led Czerny and Keller to the assumption that loss of mineral bases and the following acidosis are the prime factors in the pathogenesis of infantile malnutrition.

In the patients under our observation there was noted a considerable content of mineral bases of the feces. The fluctuations in the absolute quantities of mineral constituents removed by the feces did not follow the rise or fall in the percentage of the soap content of the feces. In Stocker (Case 3), with an average soap content of 20.3 per cent., the average ash content of the feces (weighed as sulphates) was 3.89 gm. per day, while in Janes (Case 1), with an average of 46.3 per cent., the daily output of ash (as sulphates) in the feces was 3.91 gm. per day. The absolute quantity of ash in the feces did not follow closely even the curve of the absolute quantities of soap removed through the feces; thus, in Janes (Case 1), with an average daily output of soap of below 2.0 gm., the ash output through the feces was 3.98 gm. per day, and in Dakak (Case 2) the daily output of soap was 2.7 gm. with a corresponding ash output of 2.78 gm. per day. Further, in Stocker (Case 3) a daily output of 1.41 gm. soap corresponded to 3.80 gm. of ash. This apparent paradoxic phenomenon is readily interpreted by the consideration of phosphoric acid output. A comparison of the phosphoric acid output through the feces of Janes, Dakak and Stocker (Cases 1, 2 and 3) reveals the fact that its value rises with the fall of the proportion of soap to ash. This observation is of great importance, for the reason that it demonstrates that in the chronic forms of infantile malnutrition the formation of fatty acids in the intestines does not reach the degree at which the ash content of the intestinal tract is insufficient to neutralize them. In such forms, the pathogenesis of the disease cannot be interpreted either in the light of insufficient fat absorption, or in the light of excessive loss of mineral bases, owing to the presence of unabsorbed fatty acids in the colon. The theory connecting the pathogenesis of infantile malnutrition with the phenomenon of the formation of soap stools is not applicable to conditions similar to those in our observations. Also Bahrdt[20] reached the conclusion that the quantity of fatty acids found in the patients under his observation was insufficient to neutralize all the mineral bases found in the feces. And yet in his observation the ratio of fatty acids to ash was much higher than in our patients.

MINERAL BALANCE AND ACIDOSIS

Thus the behavior of fat in the intestinal tract in chronic infantile malnutrition is insufficient to disturb markedly the salt output through

20. Bahrdt: Jahrb. f. Kinderh., 1910, lxxi, 267.

the feces and, therefore, there is little reason to expect a pronounced disturbing effect of the fat intake on the general salt balance. The analysis of the tables (Table 3) shows that in all our patients the salt balance was positive. In Janes (Case 1), who was under observation for the longest period of time, the curve of the salt balance does not follow the one of fat intake, nor that of fat absorption, nor the curve of the soap content of the feces. Thus, the behavior of fat in the intestinal tract of our patient gave no cause for creating a want of mineral bases in the tissues, nor for creating the acidosis in the organism. This hypothesis is substantiated by the analysis of the curve of the ammonia-nitrogen elimination. Only in one patient, Stocker (Case 3) the ammonia output reached the value that indicates a condition of acidosis (average = 21.3 per cent.); in all other patients, as can be seen from the tabulation below, the average ammonia output is approximately normal.

AVERAGE AMMONIA NITROGEN OUTPUT

Patient	Per cent.	Patient	Per cent.
Janes	5.6	Franco	8.3
Dakak	9.1	Vogelin	11.2
Stocker	21.3	Dolan	4.4
Guerin	6.9		

In Janes (Case 1) the fluctuations in the ammonia output do coincide with the fluctuations of the fat intake, and thus they are in harmony with the observations of Czerny and Keller,[21] Steinitz,[22] on infants, and of Schittenhelm[23] on adults.

However, similar fluctuations under the influence of alteration in the diet may occur also in health. Thus, there is no evidence that the character of the intermediary fat combustion in our patients was disturbed in a manner to cause the condition of acidosis. The exception of Stocker (Case 3) was probably conditioned by an abnormally high intestinal fermentation.

SUMMARY OF THE ANALYSIS OF THE BEHAVIOR OF FAT IN THE PATIENTS UNDER OBSERVATION

This summary brings to light the following peculiarities in the effect produced by fat intake in the seven patients under our observation:

1. In all patients it undoubtedly produced an increased peristalsis of the small intestines. Whether this effect was produced by the fat independently, or whether the fat facilitated the similar action of the carbohydrates can for the present not be stated with a degree of certainty.

2. The increased peristalsis results in a fall of fat absorption and,

21. Czerny and Keller: Jahrb. f. Kinderh., 1897, xliv, 25; 1897, xlv, 274.

22. Steinitz: Monatschr. f. Kinderh., 1902, i, 4, 225; Centralbl. f. inn. Med., 1904, xxv, 81.

23. Schittenhelm: Deutsch. Arch. f. klin. Med., 1903, lxxvii, 517.

3. In an abnormal composition of the feces, which expresses itself in a high content of insoluble soap.

However, the lack of fat absorption and the withdrawal of mineral bases by the unabsorbed fat did not reach a sufficient degree of intensity to be regarded as very important factors in causing the defective nutrition in our patients.

On the other hand, the fat of the food failed to produce the principal effect that it invariably causes in health. Namely, it failed to bring about in connection with the carbohydrate of the food the normal gain in weight in the patients, who did not suffer from any difficulty in nitrogen assimilation, and whose diet contained a sufficient amount of calories for normal growth.

In this peculiarity of fat metabolism undoubtedly is contained the principal difference of metabolism in infant malnutrition as compared with that in health. The primary cause of this abnormal form of metabolism is difficult to detect. It is conceivable that in the chronic forms of infantile malnutrition a certain vicious cycle is established. In the loss of adipose tissue caused by some disease, or by some temporary condition, the organism sustains a very grave damage of its heat regulating factors. Under these conditions a higher energy value is required for normal growth, while the average normal diet is insufficient to enable the emaciated organism to continue its growth at the normal rate. It is conceivable that the organism may grow at the expense not only of the food but also of the fat and of the carbohydrates of the reserve material within the tissues. This may last so long as the glycogen and fat from the tissues is not completely removed; after this, normal growth could be made possible only by an excessively high diet, rich in fat. Unfortunately in all of the patients under our observation, and in those recorded by other authors, there was noted a marked intolerance of the intestines for both fat and carbohydrates, which expressed itself in the appearance of increased intestinal peristalsis following a high intake of fat or carbohydrate. Therefore, in order to avoid diarrhea, both the carbohydrate and fat intake need to be limited. Under these conditions the moderate food intake can suffice for only one of the functions, either for growth or for storing up reserve material in the form of fat and carbohydrate. The tendency of the infantile organism for growth is more intense than that for storing up reserve material, and thus the organism continues to perform the function of growth under most uneconomical conditions. The continuous nitrogen retention without increase in body weight may be the expression of the condition in which growth was proceeding at the expense of the fat and carbohydrate depots. The analytical data on the composition of the tissues in infantile malnutrition furnished by

Steinitz and Weigert[24] may be regarded as supporting the view just expressed. The findings of these authors reveal a very low fat content of the tissues in this pathologic condition. The tissues of the child with infantile malnutrition contained only 2.31 per cent. fat, while according to Camerer, Jr.,[25] the normal tissues of infants of the first year contain 12.3 per cent.

It is, however, noteworthy that the deviation in the utilization of fat in infantile malnutrition is principally of a quantitative nature. The analysis of the curve representing the fluctuations in weight in Janes, indicates a certain correlation between rise in weight and increase in fat intake. It should be mentioned in this place that the possibility of nitrogen retention without a corresponding increase in the storing up of fat and carbohydrate has already been pointed out by Rubner,[26] who designated the condition by the term *"selectiver Ansatz."*

In conclusion we wish to remark that in course of the work the impression was gained that the addition of olive-oil to the usual diet in proportion of 1 to 2 per cent. of the volume of the total intake improved the utilization of the total fat. The feces returned to a composition approaching that of the normal feces, the salt balance also approached nearer the normal, and gain in weight increased in intensity. From the appended histories it can be seen that it had been employed in several cases with some promise of success.

CLINICAL HISTORIES

CASE 1.—Janes, 5 months old, was admitted to the Hospital Nov. 9, 1909. There was a history of continued loss in weight since his first month, occasional vomiting and several attacks of diarrhea during the summer. For one month before admission there was constipation and vomiting after every feeding. On admission the child was poorly nourished and had a greatly distended abdomen; weight, 4,176 grams. By November 13, the general condition had somewhat improved, digestion was better and the stools were normal.

The metabolism experiment was continued from November 17 till March 3, with interruptions, viz.: December 10 to 13; December 25 to 31; January 29 to February 14.

The weight at the beginning of the experiment was 4,134 grams. At first he appeared bright and happy. The best weight was on January 14, 4,672 grams. From January 21 to 31 there was fever, cough and a double otitis media. On this account the observations were interrupted.

On March 3, when the experiment ended, the weight was 4,261 grams, the stools thin and green, and the child did not look well. He was discharged March 7, weight 4,153 grams. Subsequent to discharge his condition improved and he gained in weight on a diet including much carbohydrate.

CASE 2.—Dakak, 7 months old, was admitted Jan. 22, 1910, with bronchopneumonia. From Sept. 14, 1909, to Jan. 20, 1910, the child had been in the hospital as a feeding case and was discharged in good condition. On readmission

24. Steinitz and Weigert: Monatsschr. f. Kinderh., 1905-6, iv, 6, p. 301.

25. Camerer, Jr.: Pfaundler-Schlossman, Handbuch der Kinderheilkunde, 1. Aufl., Leipzig, 1906.

26. Rubner: Das Problem der Lebensdauer, München and Berlin, 1908, p. 110.

he was small and poorly nourished, with signs of moderate rachitis. By February 12, the symptoms of pneumonia had disappeared; he had gained in weight and looked well.

When the metabolism experiment was begun March 8, he weighed 4,179 grams. The stools were large and good. On March 15, the metabolism experiment was discontinued, as the child again developed a pneumonia. The weight was then 4,386 grams. He grew rapidly worse and died March 21.

CASE 3.—Stocker, 3½ months old, entered the Hospital March 2, 1910. There was a history of vomiting and diarrhea for three days before admission. He was moderately well nourished; not acutely ill; abdomen distended; stools thin and yellow; weight, 4,700 grams.

The metabolism experiment lasted from March 17 through April 2. The weight fell to 4,554 grams but his general condition appeared to be better at first. The experiment was stopped April 2 because the child became weak, with loss of appetite, and the weight had fallen to 4,322 grams.

His lowest weight was 4,204 grams on April 30. The albumin of two eggs was added to his daily food. Breast feeding was attempted but he refused to take the breast. By May 27, the child appeared greatly improved; the stools were normal; weight, 4,700 grams. On June 13, olive-oil, 2 grams three times a day, was added to his food. He continued to gain in weight and was discharged June 22 in good condition.

CASE 4.—Guerin, 3 months old, was admitted Dec. 11, 1909, with symptoms of an acute gastro-enteritis. He looked acutely ill. The stools were green and thin; the weight, 4,120 grams. He improved with the addition of breast feeding.

The metabolism experiment was begun April 13 and continued until May 3. Weight at the beginning was 4,320 grams and he gained to 4,451 grams. From April 26, olive-oil was given, at first 2 grams three times, later increased to four times a day. In spite of a cervical abscess and double otitis media the child continued to gain slowly and on June 14 weighed 4,643 grams, when he was discharged.

CASE 5.—Franco, 3 months old, was admitted to the Hospital April 19, 1910, with an acute bronchitis. He was small but fairly nourished. The stools were soft and contained some mucus and often soft lumps.

The metabolism experiment was started May 7 and continued to May 31 with an interruption from May 11 to 22.

At the beginning of the experiment the child was gaining and weighed 3,593 grams. On May 11 the weight was 3,704 grams and increased to 4,002 grams by May 22. During this time four grams of salt per diem were added to the food. This was increased to five grams, but he refused the food with this added quantity of salt. At the end of the experiment the weight was 4,074 grams. On June 4, olive-oil was added, 2 grams, increased to 4 grams three times a day. The child was discharged June 17, gaining in weight and in good condition.

CASE 6.—Vogelin, 4½ months old, was admitted to the Hospital April 13, 1910. For the month before admission the stools had been green and thin and there had been constant loss in weight. On examination the child was found to be greatly emaciated, with a distended abdomen and moderate degree of rachitis. Weight, 3,794 grams. He gained steadily in weight and strength and the stools became normal.

The metabolism experiment was begun May 13 and continued only to May 16. He was very restless, cried continuously, slept very little. There was some vomiting and the stools were soft and yellow. The weight was 4,115 grams at the beginning, but in the three days had dropped to 4,040 grams. The condition became gradually worse; the stools, thin and green; there was a low fever, and a general edema; and he died on May 29.

CASE 7.—Dolan, 2 months old, first entered the Hospital Oct. 19, 1909, with pyloric stenosis. His weight was 3,058 grams. He was readmitted for several short periods until March 8, when, at the age of 7 months, the mother consented

to leave him in the hospital. At this time the weight was 3,624 grams. He was extremely emaciated, and looked acutely ill. There had been daily lavage for some time and the vomiting had practically ceased. The condition then was one of marasmus. He gradually improved during the next two months.

On April 8, olive-oil was given, 2 grams three times a day. From 3,709 grams the weight increased gradually but steadily to 4,077 grams by May 5. May 18, weight was 4,139 grams.

The metabolism experiment was then begun but he was restless and fretful and in the three days of the experiment he lost from 4,139 to 4,083 grams. During the following week, however, he gained 75 grams. On June 6, olive-oil was increased to four grams three times daily. The stools were good and the child continued to gain, weighing 4,494 grams when discharged June 21. Four months later he was still gaining.

A CONTRIBUTION TO OUR KNOWLEDGE OF THE ETIOLOGY AND NATURE OF HARD CURDS IN INFANTS' STOOLS*

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The curds that occur in the stools of infants, especially of those fed on cow's-milk, have been the subject of much discussion among pediatricians. A great deal of importance attaches to the solution of the problem of their etiology and nature, because their presence in the stools has always been considered an evidence of an overstepping of the infant's tolerance for the particular food element from which the curds were thought to be derived. The pendulum has swung from the first natural interpretation that they were undigested particles of curdled milk, therefore chiefly protein in origin, to the opposite extreme, if we are to accept the teaching of nearly all the foremost German pediatricians, that the casein takes no part in their formation. From observations that we have made in our clinic at Northwestern University Medical School, and from some experiments that I have made in the past year, I believe we are justified in stating that one extreme is nearly as far from the truth as the other.

The source of confusion lies in two places: (1) There is a lack of sharp definition of different kinds of curds; (2) German clinicians, as I hope to demonstrate, use a food that differs vitally in just this tendency to the formation of curds of a certain kind, from that which we, in this country, use as a routine. For this reason, which I will elaborate, I believe that certain curds do not occur in the experience of German pediatricians as they do in ours and that, therefore, the controversy concerning them runs in parallel rather than opposing lines.

The curds of infants' stools are distinctly of at least two kinds that differ essentially in morphology, etiology and composition:

1. The small, soft, friable, yellowish or whitish or greenish curd—the common curd of milk indigestion. This requires no further description. It has been removed from the field of discussion, almost universal consent in the last few years having given it predominatingly a fat origin. This curd occurs both when breast-milk and cow's-milk are fed.

2. The large, hard, tough curd. This curd bears no morphologic resemblance to the former, nor does it occur under similar conditions.

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*Read before the Chicago Pediatric Society, Feb. 21, 1911.

It varies in size from a mere shred or that of the head of a pin to that of a lima bean or even that of the distal phalanx of a thumb. It is commonly the size of an ordinary white bean and is generally bean-shaped, or oblong or rounded, though often, especially if very large. it is quite irregular. It is always hard and usually can be broken or crushed only with considerable force. It is of about the consistency and appearance of hard American cheese. It can be picked out of a stool with a pin or a stick, without being injured, as definitely as can a bean. So strongly is its resemblance to a soaked bean stripped of its coat that at Northwestern we commonly call them "beans," for short. On one occasion a Mr. McGuire reported at the diet kitchen that "Elizabeth wasn't doing well at all, but what could you expect when the woman was feeding it beans," and he exhibited a very convincing diaper. These curds can be washed in water with great force, shaken in water in a bottle, for example, without any tendency to disintegration, and always sink rapidly to the bottom. When separated and dried they form dry, hard, shriveled, semi-translucent masses that resemble pieces of gelatin, or of horn. Finally they crumble to a coarse crystalline powder when touched, or even crumble spontaneously.

These hard curds are either white or dough-colored, or even light greenish; or else a pale, brownish-yellow or amber color. The former are softer and more nearly friable, usually more rounded than the latter and are accompanied by a greater degree of indigestion, as shown by the occurrence of mucus and an increased number of bowel movements. The yellowish or amber-colored curds are always very hard, and can be bent without breaking. They are often accompanied by indigestion, but about as frequently occur in an otherwise nearly normal movement. The two varieties of hard curds rarely, if ever, occur together, but one kind may merge into or follow the other with the baby on an identical food, depending on whether the indigestion improves or gets worse. For this reason, and because of their striking points of resemblance, there can be no doubt that they have a common origin.

The present discussion deals wholly with these hard curds. They are distinctly rarer than the soft curds when certain kinds of food mixtures are used, distinctly more frequent when others are used, and, again, never occur when certain conditions are complied with. They do not occur in breast feeding.

The present state of our knowledge of these hard curds has recently been focused in a rather heated discussion between Fritz Talbot of Boston on the one hand, and Ludwig Meyer of Berlin, and Jerome Leopold of New York, on the other. Talbot has published a series of articles on the subject of hard curds and presents an array of evidence that has convinced him that they are of casein origin, in contradistinction to the

small, soft curds that he, too, has found to be derived chiefly from the fat. Meyer and Leopold categorically and with considerable warmth deny all of Talbot's assertions. They speak constantly of "casein masses," not, however, in the sense in which Talbot uses the term, i. e., to designate hard curds, but as a general term synonymous with curds. When Talbot in a later paper takes them to task for not clearly differentiating between small, soft and large, hard curds they emphatically refute this criticism. A careful reading of their papers in the light of my own experience convinces me, nevertheless, that Meyer and Leopold are not using the term "casein masses" as synonymous with hard curd, even when especially asserting that they do. The only possible explanation for such antagonistic opinions about so decided a phenomenon can be found in the fact that Meyer and Leopold are not practically familiar with the hard curd that Talbot, Southworth, and other American observers have described so unmistakably.

The matter assumes greater importance when we realize that in this respect Meyer and Leopold represent all of the leading German authorities, Heubner, Czerny, Finkelstein, etc.

The explanation for this lack of familiarity lies, of course, not in a lack of observation; no one would ever accuse a German pediatrician of all others, of that; but in the simple fact that these curds do not occur in their experiences, while they are common in ours, for reasons that I will elaborate presently.

The arguments that Talbot presents are, to my mind, alone convincing that these hard curds are derived from casein. The evidence that I will present will, I believe, help to clear the matter because it will enable Meyer and Leopold to make these curds experimentally, so that they too can see and study them.

That the hard curd is of casein origin seems probable from its very appearance and consistency. It is, *a priori*, almost unthinkable that it is a fat, or a salt, or a bacterial, or an intestinal secretion derivative.

Further, when fat-free milk is coagulated with rennin and then broken up, the large curds, if separated, continue to contract and express whey. They then shrivel up into hard semi-translucent, horn-like masses and finally crumble in the fingers to a coarse powder, all of which bears a striking resemblance to what takes place in these hard curds when allowed to dry in the same manner. The curd of whole milk does this less readily and remains less dry, as if dipped in butter.

Furthermore, as Talbot has shown, and as I have been able to confirm, when a mass of curdled milk is left four to six hours in 10 per cent. formaldehyde solution it becomes as hard as a billiard ball; in fact, Talbot tells us that this principle is employed in the manufacture of

billiard balls. An identical result is obtained when a hard curd is thus treated.

Microscopically, too, Talbot has shown that there is an identical appearance in hard curds and in curds made artificially by coagulating milk with rennet, and digesting the resulting curds for one hour at 98.6 F. with pepsin and 0.2 per cent. hydrochloric acid, and then, after washing, further digesting them for one and one-half hours with a fresh 25 per cent. alcoholic extract of pig's pancreas in 5 per cent. of carbonate of soda. In both natural and artificial curds there is found a white, shining, translucent network in which numbers of neutral fat drops are entangled, that evidently could not be reached by the digestive juices because of their casein envelopes. Small curds, on the other hand, as one would expect, show the fat almost entirely in the form of fatty acids and soaps.

Talbot furthermore was able to demonstrate that "curds made and digested artificially give exactly the same physical and chemical composition as natural curds." He was "able to dissolve and precipitate these tough curds, in the same way as casein, by weak alkaline and acid solutions. This precipitate was obtained in as pure a state as possible and found to contain nearly the same percentage of nitrogen as Hammerstein's pure casein."

In spite of this evidence Meyer and Leopold maintain that casein takes no part in the formation of these curds; that the nitrogen is derived from some other source, possibly, as Langstein suggests, from the intestinal secretions. Talbot then brought out a proof that these hard curds do contain casein by showing that they give a specific biologic reaction. He prepared a specific anti-cow casein serum by injecting rabbits with cow casein. With lactalbumin and human casein he obtained no precipitate with this serum, but with cow casein and with the hard curd the reaction was positive. Normal stools not containing these hard curds gave no such reaction.

That these curds are not derived from the fat of the food is demonstrated by the fact that they occur just as frequently with the use of fat-free milk as with whole milk, or cream; in fact, in my experience, for reasons that will appear later, they have occurred predominatingly with fat-free milk. In all of the experiments that I will present certified, centrifuged, fat-free milk was used.

When Czerny's chapter on *Milchnaehrschaden* first appeared we were convinced, in the light of former experiences, of the truth of its teachings concerning curds and protein digestion and increasing experience more and more confirmed the view that there was no pathologic clinical picture which could be recognized as due to casein. Prior to this time we had been followers at the clinic of the so-called percentage method of feeding.

We fed high fats and low proteins and commonly "split" the latter to get away from the "casein" curds that constantly followed us. Babies were fed almost exclusively on cream and milk and whey mixtures and while we saw innumerable small fat curds the hard curd was so rare that I, personally, had never thought of it as a distinct clinical entity. Convinced that the protein was harmless we fed it boldly in fat-free milk in almost any amount and in almost any condition and were more and more impressed with its harmlessness. The curds that we had seen so frequently formerly never appeared so long as we used fat-free milk alone.

Only one thing stood in the way of our happiness and that was the appearance in certain cases, for the first time in our experience, of an appreciable number of hard, bean-like bodies in otherwise fairly normal, fat-free milk bowel movements. After a time we noticed that these hard curds came fairly regularly when we exceeded a certain amount of fat-free milk. Personally, I came to expect them in the less tolerant cases whenever I exceeded 2 ounces of fat-free milk to the pound of baby and I gradually thought of this as almost the limit of tolerance for many cases. When the limit of tolerance was exceeded there often appeared other evidences of indigestion, the bowel movements became paler and softer, contained mucus and became noticeably more frequent. Up to this time we used raw milk practically exclusively. To counteract the diarrhea, we resorted to the time-honored expedient of boiling the milk, and found almost without exception that the digestion improved, and that *without any exception the hard curds disappeared in a day or two without otherwise altering the food.* Since that time we have nearly always boiled the milk in these less tolerant cases, always to begin with, and now again we never see the hard curd in our own experience at the clinic except as a result of a mistake in judgment. In all of our experience *we have never seen a hard curd unless a considerable amount of raw milk casein was given and we have never seen them persist or occur when boiled milk, no matter in what amount, was given.*

In a case of decomposition (Finkelstein) in which I had been feeding the patient boiled fat-free milk for some time, hard curds suddenly appeared in the stools for the first time. I expressed my regret to the mother that she had not carried out my order to boil the milk. She maintained that she had boiled it and I stated positively that the baby had had raw milk. She then suddenly remembered that in her long-extended anxiety and sleeplessness she had become absent-minded and had wholly forgotten to boil the milk on the previous day. The curds never again appeared.

To do away utterly with the possible element of coincidence I decided to make and unmake hard curds at will, in babies, by the simple expedient of using raw and boiled milk alternately. The result was as precise as

a chemical reaction in a test-tube, in each of four babies, i. e., in every baby in which it was tried.

These four babies represented different pathologic conditions and different ages. None of them was, of course, critically ill at the time of the tests themselves. They were watched with the utmost care and none of them became ill during the tests except for a slight temporary diarrhea in some of the cases. Inasmuch as the fat was eliminated and the sugar low in the foods, I felt that there was no possible danger to the babies from the serious disturbances, such as an intoxication. The remedy was always immediately at hand if a baby became only slightly ill, and inasmuch as the remedy consisted in boiling the milk the course of the experiment was not disturbed.

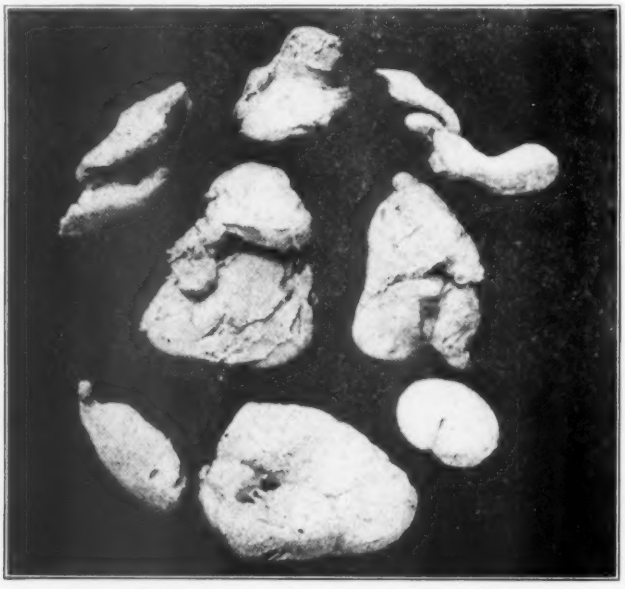

Fig. 1.—Casein curds, actual size (taken from Talbot). The curd in the lower right hand corner shows the usual size and appearance of the commonest bean-shaped hard curd. The larger ones show the indentations that appear, as though portions of the curds had been digested out. These curds are so evidently identical with those described in the text, especially to those who have seen them often, that no apology is necessary for utilizing this excellent photograph.

In every case certified, centrifuged fat-free milk was the only milk used. The reason for this was fourfold: (1) It was the food that seemed indicated therapeutically; (2) it eliminated largely the fat in determining the origin of the hard curds; (3) hard curds are made more easily with fat-free than with whole milk; (4) and most important, it eliminated practically all source of danger to the baby. Whole milk in a

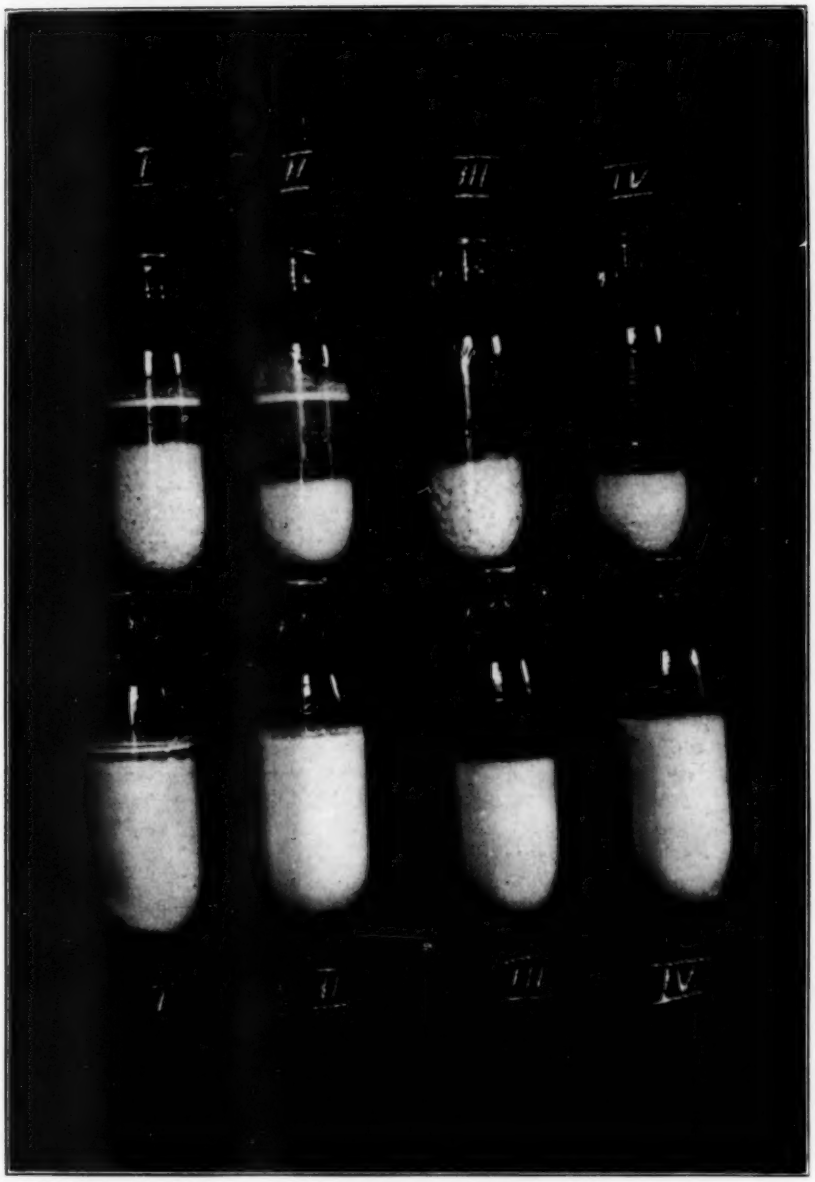

Fig. 2.—Photograph showing the effect on milk coagulation with rennin of boiling and of dilution with water. Each of the above bottles of milk was treated with the same amount of rennin (chymogen) at a temperature of 105 F. for thirty minutes, then shaken, cooled, and allowed to stand for forty hours. The upper row of bottles contained raw milk, the lower row milk that had been boiled five minutes. Bottles I contained undiluted whole milk; bottles II, equal parts of whole milk and water; bottles III, undiluted fat-free milk; bottles IV, equal parts of fat-free milk and water. Note the greater separation of whey in all the upper (raw) bottles and the coarseness of the coagulum, particularly in the undiluted bottles I and III, and especially in the undiluted, fat-free milk bottle (III). In the lower row is shown the very imperfect separation of whey, and the fineness of the coagulum when the milk is boiled, and especially when also diluted, as in bottles II and IV.

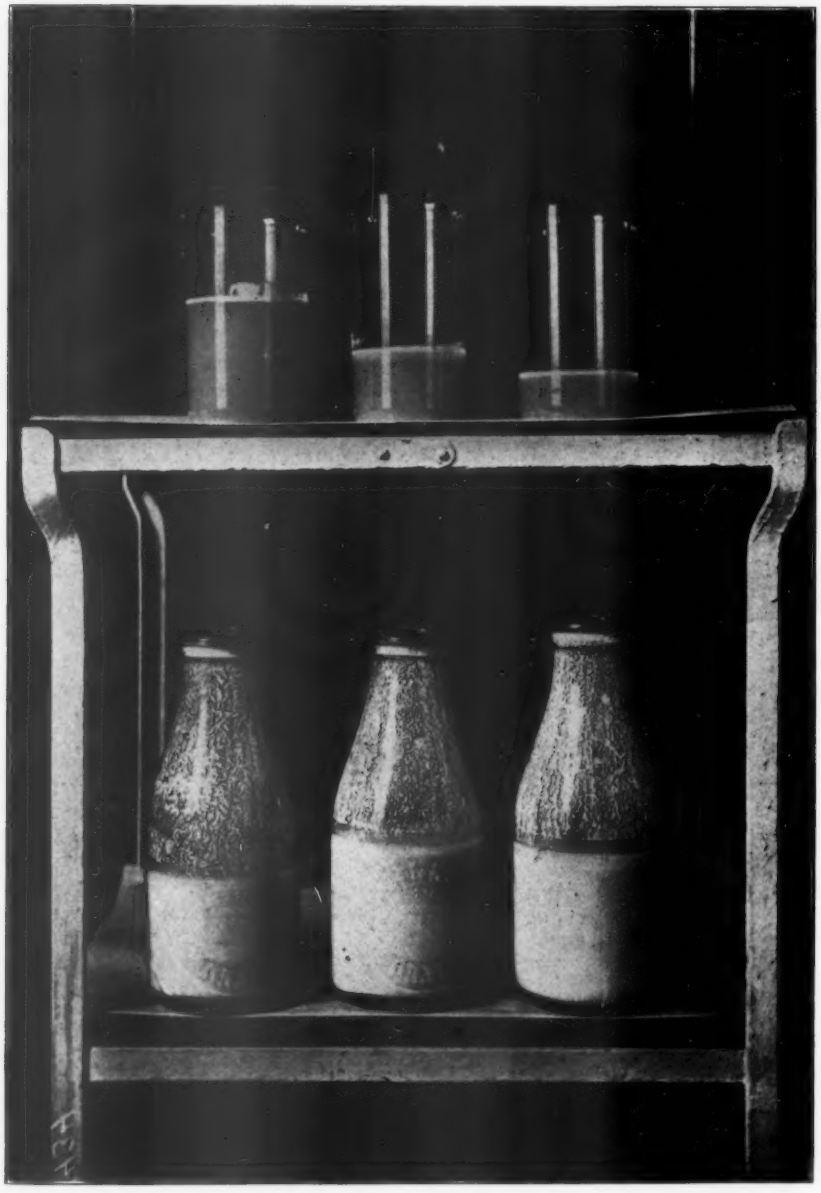

Fig. 3.—Eiweissmilch (Finkelstein) prepared with raw and boiled milk. The three quart milk bottles, from left to right, represent the amount of eiweiss-milch made according to Finkelstein's directions from one pint each of raw milk, milk just brought to a boil, and milk boiled five minutes, respectively. Above each bottle is shown the amount of whey extracted from that pint of milk. With raw milk the whey was about double, and the curd about one-half (by weight) that of the boiled milk. The difference in fineness of the curd is not evident in the photograph.

sufficient amount to give an abundance of hard curds would probably have produced many small fat-curds, or a soap stool, or would have been a serious menace to an atrophic infant. The fact that none of the babies suffered in any way beyond a slight temporary indigestion demonstrates again the insignificance of the rôle played by the proteins in nutritional disturbances as compared with the fat or the sugar. When the milk was boiled this was done in a single boiler for two to five minutes. In every instance the food was begun at 4 p. m., the stools inspected the next forenoon, and a day corresponded to a calendar day.

It will be necessary to give these cases in sufficient detail to show the conclusiveness of the evidence.

CASE REPORTS

CASE 1.—Baby B., aged 4 months, weight 10 pounds 5 ounces; nursed two months, then fed cow's-milk whenever it cried, had been sick ever since; had five to six dyspeptic stools a day. The baby had a typical, profound intoxication (Finkelstein), with low fever.

The patient entered Wesley Hospital Oct. 7, 1910, and was put on *boiled* fat-free cow's-milk, 15 ounces, barley water, 15 ounces, for three days. In the next two weeks the food was gradually increased to fat-free cow's-milk (*boiled*), 22 ounces, and human milk, 10 ounces a day. In the first week there were five to nine dyspeptic stools a day and the child was generally edematous, with dry, hard, leathery skin and tissues. During the second week these symptoms all disappeared, the look of intoxication was no longer present, the digestion became normal, the baby had one or two stools a day and gained 2 ounces. Up to this time the cow's-milk was always boiled and no curds had appeared.

October 20. *The milk was now ordered raw* and consisted of fat-free cow's-milk, 22 ounces, human milk, 5 ounces, barley water, 13 ounces, flour-ball, ¾ ounce.

October 21. One normal stool, no curds.

October 22. Two stools, one at 1 a. m. contained one hard curd and a later stool had three large, white hard curds the size of small lima beans. The first curd appeared thirty-three hours after food was given raw.

October 23. Four stools containing hard curds.

October 24. Seven stools each containing large, hard, whitish curds varying in size from a small pea to a large marble, or filbert, and forming often apparently more than one-half of the bulk of the movement. The rest of the stool was liquid and greenish.

Because curds often appear more freely when undiluted milk is given, to eliminate further the additional carbohydrate, and for more accurate experimental purposes, the baby was now put on 30 ounces of raw undiluted fat free milk.

October 25. Five stools of same consistency, each containing large, white, hard curds. The same food was now given boiled five minutes.

October 26. Five loose, somewhat greenish stools; 2 a. m. stool had a few yellow or amber-colored curds the size of a split pea. Baby looked better.

October 27. Four stools. Two contained hard curds, one a few small yellow ones; the other has several larger and a number of smaller yellow curds. No more curds after the 12:30 stool, i. e., forty-four hours after the milk was boiled.

The baby was kept on this same fat-free milk, 30 ounces, for six days. It had four or five thin but greatly improved stools a day, in none of which were there any curds. Baby in good condition.

November 2. Same food, 30 ounces fat free milk again ordered raw.

November 3. Four stools; fourteen hours after beginning raw milk one stool contained many typical, large, whitish curds the size of a lima bean.

November 4. Four stools. One contained one very large, hard curd; the rest all had several small, yellow, hard curds.

November 5, 6 and 7. During these three days the baby had four and five stools a day, some of which each day contained small and large yellow hard curds. The food was then changed to whole cow's milk, 12 ounces, barley water, 18 ounces, boiled five minutes.

November 8. Four stools. Two large yellow curds in the morning stool, none after that. During the next four days ½ ounce of a malt food was gradually added to the food. The stools became normal, rather constipated, with no curds of any kind at any time. The baby left the hospital five days later in excellent condition, having lost only 11 ounces in spite of the severe intoxication and edema at the start.

In this baby we felt in advance, on account of its age and recent dyspepsia, that we had a favorable case for large curd formation. The large, white curds of the first trial were an evidence of a severer reaction; the smaller, yellow, harder curds of the second trial showed that the child's ability to handle an excessive amount of raw fat-free milk had improved greatly. Especial interest attaches to the fact that in spite of the sudden addition of a considerable amount of fat in the 12 ounces of whole milk, and of carbohydrate in the form of barley water and malt food, no more curds appeared when the milk was boiled five minutes.

CASE 2.—Baby W., entered Wesley Hospital Nov. 20, 1910. Age 5½ months, weight 7½ pounds; had lost 6 pounds; breast-fed one and one-half months; then a fine fat baby. The infant was then put on various foods, finally on pasteurized cow's-milk. It was always extremely constipated, so that it had marked prolapse of the rectum.

Diagnosis, simple malnutrition. On account of the good digestion and marked constipation the baby seemed especially favorable, because it would not be likely to be acutely upset.

From Nov. 30, 1910, to Jan. 20, 1911, the infant was given various whole-milk, fat-free-milk and human-milk mixtures with carbohydrate additions. The cow's-milk was always boiled. The child was so constipated that commonly ½ ounce of milk of magnesia was added to the food. *For one month the baby was now kept on the same food, 30 ounces of fat-free milk, daily.*

January 20. Put on fat-free milk, 30 ounces, boiled five minutes.

January 21. Two stools. No curds.

January 22. One stool, constipated, no curds.

January 23. Two normal fat-free milk stools. No curds. Milk ordered raw.

January 24. One stool, dry and constipated. No curds.

January 25. One lighter, softer, stool containing many small yellowish bean-like curds, about thirty-two hours after raw milk was started.

January 26. Two stools. Each had large and small, hard, yellow curds, larger than on the previous day.

January 27. Two stools. First had six or seven small, yellow curds; second had more hard yellow curds than any previous stool.

January 28. No stool. Milk boiled two minutes.

January 29. Two stools. Three hard yellow curds. None after twenty-four hours of boiled milk.

January 30. One stool. Very constipated. Stool like marbles. No curds.

January 31. Two stools. No curds. Same food again ordered raw.

February 1. One stool. Seven large and small yellow curds within fourteen hours of giving raw milk.

February 2. One stool softer and paler; seven yellow curds of medium size.

February 3. One stool; seven yellow curds.

February 4. One stool; eleven yellow curds, some quite large. Sodium citrate, gr. xxx, added to the same raw milk.

February 5. One stool; same number and size of curds.

February 6. One stool; same color and consistency. One large and two small yellow curds.

February 7. One stool, same as before, contained six yellow curds. Sodium citrate, gr. lx, added to same milk raw.

February 8. Two stools. First, at 10 a. m., had seven or eight very small, yellow curds; second, in the afternoon, contained no curds. Sodium citrate reduced to 30 grains.

February 9. One stool; one large and several smaller hard yellow curds. Sodium citrate again increased to 60 grains.

February 10. One stool; six very small, yellow curds.

February 11. One stool; no curds. Curds ceased as before in twenty-four hours when sodium citrate was increased from 30 to 60 grains. Sodium citrate omitted. Milk still given raw.

February 12. One stool; first part hard and contained no curds.

Last part of same stool was softer and contained two yellow curds.

February 13. Two stools; each contained several hard, yellow curds, one very large.

February 14. One stool; contained a number of very large, hard, yellow curds and several smaller ones. Milk ordered boiled two minutes.

February 15. One stool; two large and three small yellow curds.

February 16. One stool. No curds. Same milk ordered raw.

February 17. Two stools. One early a. m. had no curds. One at 7 p. m. contained twenty to thirty large and small hard, yellow curds.

February 18. One stool liquid, pale yellow. About twenty medium and small, paler yellow, nearly whitish, softer, hard curds. Milk at once given boiled two minutes, because of the condition of the movements.

February 19. Two stools. One at 2 p. m. had several small, harder, yellow curds. Second at 9 p. m. contained one very small curd the size of two pinheads and several shreds.

February 20. No stool.

February 21. Two stools, no curds; baby in good condition.

A special point of interest in this case is the fact that when enough sodium citrate was given its action in stopping the formation of curds was identical with that of boiling the milk.

CASE 3.—Baby S, aged 23 months; weight 14 pounds; undersized child with typical *Milchnaehrschaden* (Czerny); typical soap stools. In this case I had considerable misgiving as to our ability to produce hard curds at all, on account of the child's age and good digestion and I felt that large amounts of undiluted fat-free milk would have to be given to reach the desired result.

October 17. The child entered Wesley Hospital and was given water until the following morning.

October 18. The following food was ordered: Fat-free milk, boiled, 18 ounces, barley water, 18 ounces, flour-ball, ½ ounce.

October 19 and 20. Child normal in every way. Food increased to fat-free milk (raw). 28 ounces, barley water, 8 ounces, flour-ball, ½ ounce.

October 21 and 22. Bowels rather constipated; no curds; food increased to fat-free milk (raw), 32 ounces, barley water, 10 ounces, flour-ball, ½ ounce.

October 23 and 24. No change of any kind. Food now limited to fat-free milk 48 ounces raw.

October 27. Sixty hours later one or two stools contained yellow, hard curds.

October 28. Three stools with several large bean-like, yellow curds in one of them.

The child was now put on whole milk, raw, 10 ounces, fat-free milk, raw, 23 ounces, barley water, 15 ounces, flour-ball, 1 ounce, thus adding fat, increasing

the carbohydrates and lowering the protein and salts only. For the next eight days the child had daily from one to two movements that were well digested and contained no curds. The food during this time was gradually increased to whole milk (raw), 20 ounces, fat-free milk (raw), 13 ounces, barley water 15 ounces, flour-ball, 1½ ounces. This, together with some additional soft food, brought on a slight diarrhea, with three to five stools daily on November 6, 7 and 8, and on the 9th there again appeared several yellow, hard curds. The same food was now boiled; the digestion quickly became normal in every way and no more curds were found. The child gained 2 pounds during the four weeks in the hospital. At no time were the curds abundant, but they were morphologically identical with those of the previous baby and were always, as one might expect, of the hard, yellow type that accompanies less severe disturbances.

CASE 4.—Baby K., 6 months old, weight 11 pounds; very pale; simple malnutrition; no stool for first forty-eight hours in the hospital. The infant entered Wesley Hospital Oct. 16, 1910, and was given fat-free milk boiled 5 minutes, 15 ounces, barley water, 15 ounces, flour-ball, ½ ounce.

October 17, 18 and 19. One movement daily, normal in every way.

October 19. Same food ordered given raw.

October 20. Stools normal with enema. Fat-free milk raw increased to 22 ounces; food otherwise the same.

October 21. One normal stool.

October 22. Four stools. Nearly all of them contained a number of yellow, hard curds. Food increased to fat-free milk (raw), 24 ounces, barley water, 12 ounces, flour-ball, ½ ounce.

October 23. Three stools, containing some curds as before.

October 24. Four stools, no curds.

October 25. Five stools. Only one of these contained small yellow curds.

October 26. Three stools, with a few small yellow curds. As in the previous cases the food was now changed to undiluted raw fat-free milk—in this case 36 ounces.

October 27. Six stools. Last one contained several yellow curds.

October 28. Five stools. One contained several small bean-like yellow curds.

October 29. Three stools. First one contained several large yellow curds.

October 30 and November 1 and 2. Five, two and five stools, respectively. No curds.

November 2. Five stools. A few yellow curds in one of them. Milk now ordered boiled.

November 3. Five stools. One curd in one of them.

November 4. Five stools. No curds except a few the size of a pin head in one of them. No more curds after that, even when put on whole milk (boiled), 12 ounces, barley water, 18 ounces.

The infant left the hospital November 21, in good condition. In this case the baby was older and heavier than baby B, had no digestive disturbance to begin with, and its ability to handle a large amount of raw, fat-free milk was much greater, as shown by the fact that the curds were never abundant, were always of the hard, yellow type, and even showed a tendency to disappear while on raw milk. A larger amount of raw milk would doubtless have caused more curds to appear, but the frequency of the stools did not warrant such a procedure.

Having now demonstrated that in all of the cases in which it has been tried (and one would hardly be justified in trying it on more cases, even though the experiment is harmless), hard curds have been made to appear when a sufficient amount of fat-free milk was given raw, and made to disappear, without an exception, when the milk was boiled, I believe one is justified in making a general application of this fact, especially so when

combined with our former extensive collective experience at Northwestern, in which the same condition was always found.

That whole milk will produce the same hard curds will be doubted only by one who has never seen identical hard curds when whole milk was fed raw. That they occur only infrequently when whole milk or cream mixtures are used is easily explained by the fact that nearly always the fat or the added carbohydrate will produce serious disturbances long before so small an amount of casein, if we may accept this as the origin of hard curds, will produce any changes. Then too, on account of its greater food value, whole milk is used in less amount than fat-free milk would be for the same baby. For reasons which will appear later, it is very probable that hard curds are formed more readily with fat-free milk than with whole milk or cream. For curds to appear in fairly normal babies the raw milk must be excessive; the more nearly undiluted the more likely are curds to appear; or the baby must be in a condition that cannot yet be defined sharply in which it cannot handle even a small amount of raw milk. Thus in the two more delicate cases, Baby B. and Baby K., curds began to appear when 2 ounces af raw, fat-free milk to the pound of baby were given. In Baby W., which seemed to have a better digestive capacity in every way, curds appeared with 3 ounces, and in the older child, Baby S., with a practically normal digestion, even 3½ were required.

An explanation of the phenomena I have described does not seem hard to find. In the last year I have made a large number of experiments to determine the difference, *in vitro,* of raw and boiled milk in the presence of rennin. This difference, in a general way, is familiar to all of us, and yet we have not been sufficiently impressed with it, nor have we made such practical applications as readily suggest themselves. I will give in a general way only those features of these experiments that have bearing on the main point here at issue.

Undiluted raw milk when treated with rennin at body temperature will thicken in a few minutes, will then form a firm, hard jelly that will hardly fall from the inverted beaker. This clot then contracts to a smaller bulk while whey is separated from it. If broken up with a spoon at the end of fifteen to thirty minutes there will be a definite separation of large cheesy curds, and a more or less clear whey. If the curds are separated from the whey and set aside it will be found that they naturally keep on contracting with the further expression of whey. They soon become as hard as the white of a hard-boiled egg. If allowed to dry longer they finally resemble pieces of hard gelatin or horn, very strikingly like the hard curd dried in a similar manner.

If, now, undiluted cow's milk that has been boiled for five minutes is treated in the same manner, very significant differences are soon appar-

ent. Coagulation is not only greatly delayed, but even at the end of half an hour at a temperature of 100 to 105 F. the curd is very soft and friable, about like a good custard. When this is now broken up as before with a spoon there is no marked separation of hard curd and whey, but the whole mixture still looks like a thick, fluid milk, about the consistency of buttermilk. On drinking it one notices only a slight thickening of the milk; distinct curds are not evident.

If the experiment is repeated with diluted raw milk, say equal parts of raw milk and water, a further striking change is noted. Coagulation is much retarded and the resulting curd is less firm and tough. Nevertheless, when the coagulum is beaten up the mixture will consist, as before, of firm separated curds, less tough, however, than when undiluted milk is used, and whey. If an identical dilution of milk and water is boiled for five minutes and then treated with rennin, there is almost no perceptible coagulation and only the slightest thickening, even at the end of thirty minutes.

With other dilutions, and with different lengths of time of boiling, the following general principle is established: The more milk is boiled, or the more it is diluted, the slower the coagulation and the less firm the coagulum. Or, in other words, the rapidity of formation and the firmness of the coagulum vary directly with the amount of casein, and inversely with the length of time of boiling. Milk diluted more than one-half and boiled ten or fifteen minutes is practically non-coagulable with rennin in such amounts as was used in these experiments. Pasteurized milk acts in this respect like raw milk.

When fat-free milk is used in these experiments instead of whole milk the resulting curd is tougher (almost leathery when the milk is raw and undiluted) than with whole milk. When dried this same thing is equally true; the resulting curd from raw, undiluted, fat-free milk is nearly white and becomes hard as bone, long before the yellower, softer, more friable, greasy, whole milk curd has become nearly so hard. The latter is doubtless due to the fat held in the casein. Ultimately when continued drying takes place these curds will crumble between the fingers into a coarse crystalline powder just as do the hard curds from the stools. In both natural and artificially made hard curds Talbot found further that the fat content varied directly with the amount of the fat in the food and in the milk from which the artificial curds are made, respectively.

In vitro, then, if we thought of the contents as food, raw milk and especially raw fat-free milk would be considered a mixture of a solid and a liquid food, and boiled milk would be a liquid food, very similar in this respect to an infant's natural food.

But we are told by Czerny that deductions made from what goes on in the beaker cannot be applied to conditions in the stomach. He states, furthermore, that if the milk is constantly stirred or agitated in a beaker firm coagulation cannot take place.

Simply to confirm this finding I did the following experiment and was astonished at the result. In four beakers containing 4 ounces each of undiluted, whole, raw milk, undiluted whole milk boiled five minutes, undiluted fat-free milk raw, and undiluted fat-free milk boiled five minutes, I placed the same amount of chymogen (about 7½ grains) and kept them at a temperature of 100 to 105 F. for fifteen minutes. Duplicates of each of these were made and while the one set was allowed to coagulate undisturbed, the other set was constantly and vigorously stirred with a spoon. At the end of fifteen minutes the contents of each of the eight beakers was stirred vigorously.

In the case of the undiluted, raw, fat-free milk that was stirred constantly the separation of curd and whey was most complete and the curds were large, from a pea to a marble in size, and were more tough and leathery or rubbery than I had ever seen them before, while in the undiluted, fat-free milk not stirred the separation was less complete, and the curds smaller and much more easily divisible. In the raw whole milk the difference was even more striking, possibly due to the fact that some one else stirred this beaker and may have used more of a rotary than a criss-cross motion. In the unstirred beaker the separation was fairly complete, but the whey was milkier, while the curd was quite firm but still easily divided into smaller curds on stirring. In the beaker that was stirred constantly the whey was very milky and practically all of the curd was in one tough ball nearly the size of a walnut.

In the boiled, undiluted, whole milk beaker that was unstirred, the mixture after stirring at the end of fifteen minutes was simply a thickened milk in which one could not recognize separate curds on testing it. In that which was stirred the milk showed a distinct tendency to separation into a paler solution containing small easily visible and tastable, rather firm curds, about the size of a pin-head. In the boiled, fat-free milk beakers there was the same condition, only the curds were tougher, and the milk was decidedly gritty to the taste in the stirred beaker.

Each of the eight beakers of milk treated as an unknown could at once be recognized and especially *could the stirred milk in each case be distinguished from the unstirred milk on account of the greater distinctness, size and firmness of the curd.*

One can only agree with Czerny that the conditions *in vitro* and in the stomach are probably different, but it would be as easy from this experiment to conclude that motion favors hard curdling, as to deduce from his experiments that curdling is inhibited. Fortunately we do not

need laboratory experiments to convince us that milk can curdle in the stomach in large, hard clots. Those of us who have fed raw milk have repeatedly seen infants with disturbed gastric digestion, if I may use the term, vomit firm, leathery curds larger than the end phalanx of a large thumb. Czerny probably has not seen these large stomach curds because he uses boiled milk exclusively.

It seems to me, then, quite plausible that tough curds are formed in the stomach of an infant when fed raw milk; experimentally, in a healthy infant when the casein is excessive and especially when undiluted, and clinically in a dyspeptic infant when its tolerance for raw casein is overstepped, no matter how small an amount is given; and that these hard curds are resistant to digestive liquefaction and pass through the intestinal tract without complete disintegration. This is evidenced by the fact that the curds, when there is considerable diarrhea, are passed through rapidly and are abundant and whiter and softer, and when the baby is constipated they are more yellow and always harder, as if they had had a longer time to express whey content and also a more prolonged exposure to the digestive juice, leading to a reduction in size. These harder curds often look as if they had had holes digested into them while the softer ones are nearly always more rounded and even.

Tobler has stated that "it is highly improbable that such a casein mass should pass through the whole intestinal tract undigested." It is hard to see why such tough curds as we have seen in the test-tube and as we have seen vomited from an infant's stomach, should not pass through as undigested as other pieces of all kinds of solid food, that we are familiar with in infant and adult. It is quite inconceivable, it is true, that any casein curd from boiled milk could pass through undigested.

That such large bodies can easily pass the pylorus is shown in the cases where pennies, safety-pins, marbles and what not are passed.

That the presence of hard curds in the stools is due to the formation of large curds in the stomach seems further highly probable when we know that they will disappear as well when enough sodium citrate is added to the milk as when it is boiled (see case of Baby W.). Milk treated with sodium citrate acts in the test-tube like boiled milk as far as coagulation is concerned, and it is reasonable to assume that it is the lack of firm coagulation in the stomach that causes the curds to disappear in both cases.

German pediatricians use boiled milk in feeding their babies. We, in America, use raw milk almost as much, as a routine, as they do boiled milk. How deeply the hobgoblin of scorbutus has influenced us is shown even in the attitude of the mothers, who immediately wonder if they have called the right physician to see the baby if he asks to have its milk boiled, even if only for a few days. It seems to me then, that, for the above

reasons, we are justified in concluding that these hard curds do not occur in Germany while they are not uncommon with us. If they did occur there they long ago would have been accurately described (and the descriptions of "casein masses" by German clinicians are certainly indefinite now as compared with Talbot's and mine), they would have been analyzed, their origin determined and the present controversy would not have been continued nor so heated. The very impatience with which Meyer and Leopold deny all that Talbot claims, while it seems so plausible to us, can hardly be explained on any other basis than that they do not see these hard curds as we do.

Hard curds, are, furthermore, evidently a digestive disturbing factor, and the arguments of Meyer and Leopold, based on metabolism, to show the harmlessness of casein, are wholly beside the question. It is easy to agree with these observers that boiled casein produces no digestive or metabolic disturbance that is recognizable at present, but raw casein in milk can produce a digestive disturbance, in that hard curds may occur when it is fed.

The question of protein digestion, so recently settled for many of us by Heubner, Czerny and Finkelstein, and their schools, if the above conclusions are warranted by the evidence, must be opened again. As shown above, when hard curds appear in the stools, depending wholly on the baby or on the amount of casein given in raw milk, other evidences of indigestion commonly appear. If the same food is boiled, commonly all of the symptoms of indigestion disappear as well as the curds. Whether the curds are an evidence of a primary protein indigestion, secondarily causing mechanical or other irritation; or whether they are an accompaniment of some other digestive disturbance caused by feeding raw milk, just as mucus, curds, increased peristalsis, etc., accompany, say, a dose of castor oil, remains to be determined. It seems to me that these hard curds must be given the same weight as an evidence of casein indigestion that is given to the small soft curds, as an evidence of fat indigestion, although the two processes are wholly different.

Practically, that is, clinically, one's conclusions concerning protein digestion in feeding cow's-milk are but little influenced by the evidence that I have presented, that under certain limited conditions casein may appear undigested in the infant's stool as hard curds. In the experiments that I have given the hard curds were in reality an artefact. Even in the use of diluted, raw, whole milk mixtures as commonly used, these curds rarely appear unless the baby is given a larger amount of milk than it should have; i. e., when a baby is improperly fed. Indeed, even when hard curds appear, under these conditions, it is probable in many cases that the fat or the carbohydrate has produced an indigestion, and the hard curds are simply a result of an increased peristalsis that has

swept them through before they could be digested completely. The appearance of these hard curds, when proper amounts of raw milk are used, will be limited very largely to those patients who are getting fat-free milk, and to a very small percentage of patients in whom, for some reason, there is a peculiar temporary susceptibility to casein indigestion. There is some evidence in my experience that raw milk will at times produce colic, or discomfort that is relieved by boiling the milk. Even in an adult I have known 24 ounces of raw milk repeatedly to produce colicky pains and even a slight diarrhea, while the same amount of boiled milk under identical conditions never causes discomfort. Even when raw milk is used in therapeutic amounts, we must conclude, in spite of these isolated cases, that the dictum that casein produces neither digestive nor metabolic disturbance is very nearly true. Certainly it would be wholly unjustifiable to speak of it as belonging, as a disturbing factor in infant feeding, even remotely in the same class as the fat or the sugar.

In this paper I am offering no therapeutic suggestion of any kind with reference to whether milk should commonly be boiled or not. I cannot refrain from saying a word, however, concerning certain therapeutic measures. Certain very diverse foods, commonly recognized as easily digested foods, such as buttermilk, condensed milk, dried milks, sodium citrated or otherwise alkalinized milks, all have one thing in common—they do not curdle in hard masses as raw milk does.

On the other hand, it is certainly a question whether the use of rennin, as in pegnin, or chymogen, has decided, or, indeed, any advantages when the milk is previously boiled, over boiled milk itself; and when not boiled the result is not satisfactory because of the toughness of the small curds that are formed.

Even in the preparation of *Eiweissmilch*, with raw and boiled milk, respectively, there is an appreciable difference in the consistency and amount of the curd and the amount of whey extracted; hence a difference in the ultimate food itself in the very respect that makes it unique and effective as a therapeutic measure. He who uses raw *Eiweissmilch* will get very different results from another who uses boiled milk in its preparation. The fact that Finkelstein, Langstein and Meyer make no reference to whether boiled or raw milk should be used in preparing this food, shows how little German pediatricians appreciate this great difference between raw and boiled milk, or rather how unfamiliar, *practically*, they are with the use of raw milk as an infant food and with the one evident digestive disturbance that it occasionally causes, i. e., the formation of hard curds.

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A DUODENAL TUBE FOR INFANTS

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During the past few months two tubes have been devised which may be introduced by mouth and passed into the stomach and thence into the duodenum. The description of these tubes was published almost simultaneously by Gross[1] and by Einhorn.[2] Both instruments, however, were constructed for use on adults, and both seem to have accomplished their purposes, although they differ somewhat in principle. It seemed to me that it would be well worth while to devise a similar tube for infants, and accordingly I have endeavored to modify and, as I believe I can demonstrate, have succeeded in so modifying the Gross tube that it can readily be adopted for use in the field of pediatrics. I believe that this tube will be of practical use in the treatment of infants, and may serve also to give additional information in those unexplained cases of malnutrition with which we constantly are confronted.

In this paper I do not intend to do more than give a simple description of the tube, to prove that it in reality reaches the duodenum, to describe its method of introduction, and in the briefest way, to indicate its possible uses. In a subsequent article I hope to consider in detail its clinical application, and to report on the duodenal juice in infancy in normal and pathologic conditions, a study that is now under way. The principle of the duodenal tube which I present consists in having a heavy metal ball attached to the end of a very light tube so that it will be quickly carried by the aid of gravity through the stomach and the pylorus.

The tube shown in the accompanying illustration (Fig. 1) is made of very soft, light rubber, 5 mm. in diameter, and has at one end a silver-plated lead ball. The ball is perforated by numerous small openings and one large central one, and is covered over by the end of the tube, which has corresponding perforations. The diameter of the rubber-covered metal ball is 9 mm.

In this connection I would say that I found it most difficult to ascertain the size of the lumen of the pylorus in the various ages of infancy. The figures given in studies on this subject, for example that of Pfaundler, have as a basis measurements made on the cadaver, and have the usual limitations of statistics obtained in this way. By trying balls of different sizes I found that one of 9 mm. gave in general the best results. A ball

1. Gross, M.: Jour. Am. Med. Assn., April 23, 1910.
2. Einhorn, M.: Med. Rec., New York, Jan. 15, 1910.

of 6 mm., for instance, will not be carried so quickly through the pylorus by gravity and takes a longer time to enter the duodenum.* Beside the tube, I used the same glass collecting bulb which is made use of with the tube for adults.

TECHNIC

The preparation of the infant for duodenal aspiration consists merely in enveloping it snugly in a sheet or in a blanket in such a way that the hands cannot be freed to grasp the tube. The time most suited for introducing the tube, if an uncontaminated juice is desired, is two or three hours after the last feeding; that is, when the stomach is empty. If it is not performed, for one reason or another, at this time, and if the infant has just been fed, I have found it of advantage to empty the

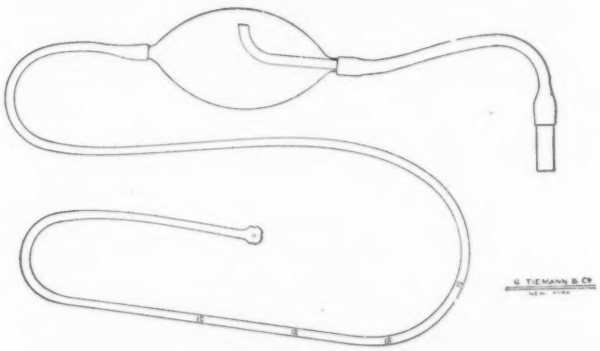

Fig. 1.—Duodenal tube for use in infants, with metal ball and glass bulb, for aspiration and collection of duodenal juice.

stomach with an ordinary stomach-tube as a preliminary step, and in this way avoid all possibility of clogging the small holes in the ball by means of milk coagula. The tube is introduced with the infant held in the sitting position, the method being in no way different from that followed in passing the stomach-tube. The advent of stomach contents, milk or gastric juice will inform us when the ball has reached the stomach; this will be found to be when it is about 18 to 20 cm. distant from the lips. The child is now placed on its right side, and the tube introduced 5 cm. farther, until the 25 cm. mark is at the lips. From this point on, the object is to feed the tube little by little until it reaches and passes the pylorus. If it is fed too fast there is danger of its doubling on itself, with failure as the result. In this regard a little practice is necessary, but after a few attempts a sense of precision is gained. If the tube is pushed farther every few minutes the peristaltic action of the stomach will be felt to aid

*Smaller infants frequently cannot swallow the larger ball, and we have to resort to the 6 mm. ball, which gives the same result, but is more easily clogged by the viscid juice or extraneous particles.

in carrying it along. After fifteen minutes the 30 cm. mark should be at the lips, and about ten minutes later, it should have advanced to between 30 and 35 cm., which means that it is in the duodenum. No rigid schedule can of course be outlined in this connection. I have reached the duodenum within ten minutes and usually am able to enter it within twenty minutes after I have introduced the tube. In one very small, weak infant, I failed to pass the tube.

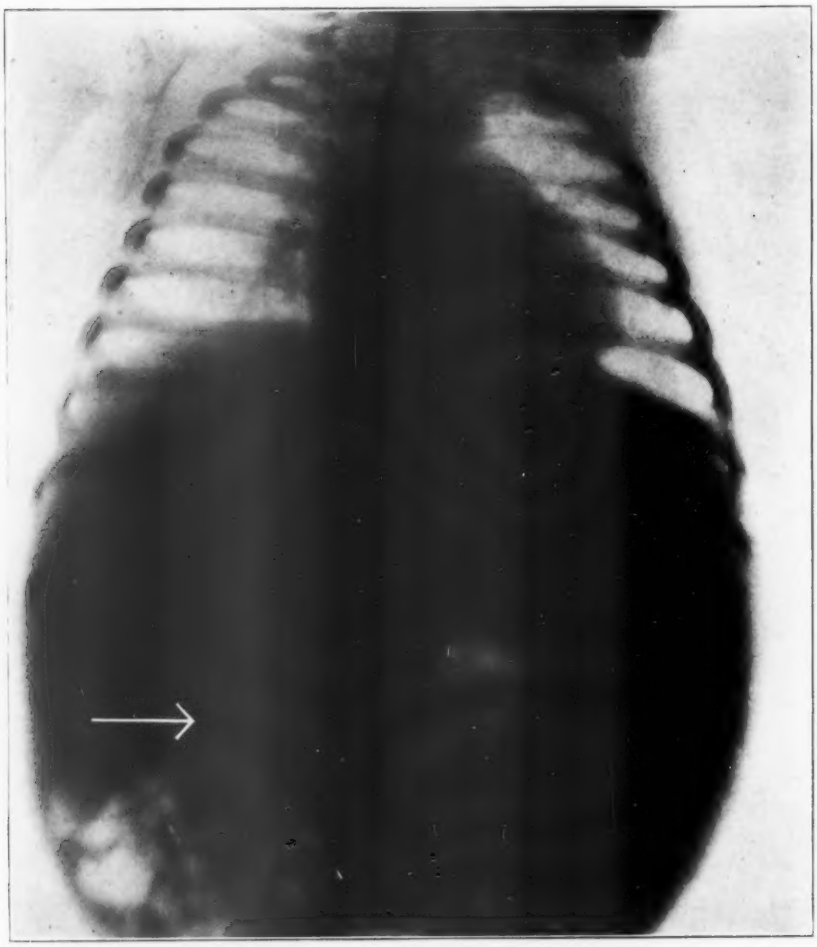

Fig. 2.—Radiograph showing tube and metal ball well within the duodenum as indicated by the arrow.

The first question generally asked is: How do we know that it is in the duodenum? Before answering this I wish to refer to the two plates (Figs. 2 and 3) which are taken from radiographs kindly made for me by Dr. Hirsch, of a 1-year-old infant on the service of Dr. Huber, in Beth

Israel Hospital. The first (Fig. 2) shows the tube and metal ball well in the duodenum, having curved down into the upper intestine after traversing the stomach. For the purpose of obtaining a clear shadow a small rubber tube infiltrated with lead was inserted into the duodenal tube before it was passed on the infant. In order to dispel any doubt as to the whereabouts of the end of the tube, after this radiograph was taken I then poured a suspension of bismuth in milk along the tube into the stomach. Figure 3 shows the stomach partly filled with this bismuth, which has within a few minutes passed also into the duodenum, and portrays the ball of the tube in the duodenum as in the previous radiograph. These pictures are conclusive; they prove that a tube can be passed through the mouth into the intestine of an infant. However, the character of the juice which is aspirated will also generally give the signal that the duodenum has been reached. At first, when the tube is in the stomach, the aspirated fluid is markedly acid to litmus, and contains flocculi of milk. It may become still more acid if the secretion of gastric juice is stimulated. When the ball reaches the duodenum, the juice becomes less acid, the acidity gradually diminishing until it becomes neutral or slightly alkaline. Generally it has a characteristic viscid consistency and a yellowish or greenish tinge, which is rather difficult to perceive by artificial light. This color is due to a mixture of bile, and varies from a golden yellow to a tinge of yellow or green; or the fluid may be colorless although the tube has passed through the pylorus, and its end lies beyond the papilla of the bile duct. The fluid is generally not absolutely clear, but contains small flocculi which tend to fall to the bottom of the glass as sediment. The characteristic fluid, the only fluid which we can use as a criterion that we are in the duodenum, is one that is neutral or alkaline, and shows a definite yellow or green color.

In the accompanying illustration (Fig. 1) it will be noted that a glass bulb is attached to the outer end of the tube, and that this again has a small piece of tubing attached to it. This bulb is to serve as a container for the juice that is collected, and the tube at its end is for the purpose of aspiration.

The aspiration may be made by the mouth, the method that I have followed, or by means of a syringe. Aspiration is generally necessary, as the juice does not at all times flow freely, and the tube may be choked by particles of milk. This procedure should be carried out gently and not too often, as it has a tendency to cause retching and gagging. As can be imagined, there are many minor details of technic which might be mentioned, but the mode of introduction is simple, so that these finer points may be left to suggest themselves to those who make use of the tube.

A word as to the discomfort which the passage of the tube entails. I need not mention that it can cause no injury, for we all acknowledge that the stomach tube is used with perfect safety and the soft duodenal tube, in this respect, can be, and is in no way different. I have passed the tube in infants varying in age from 2 months to 14 months (the smallest infant weighed 7 pounds) and found that it did not cause much discom-

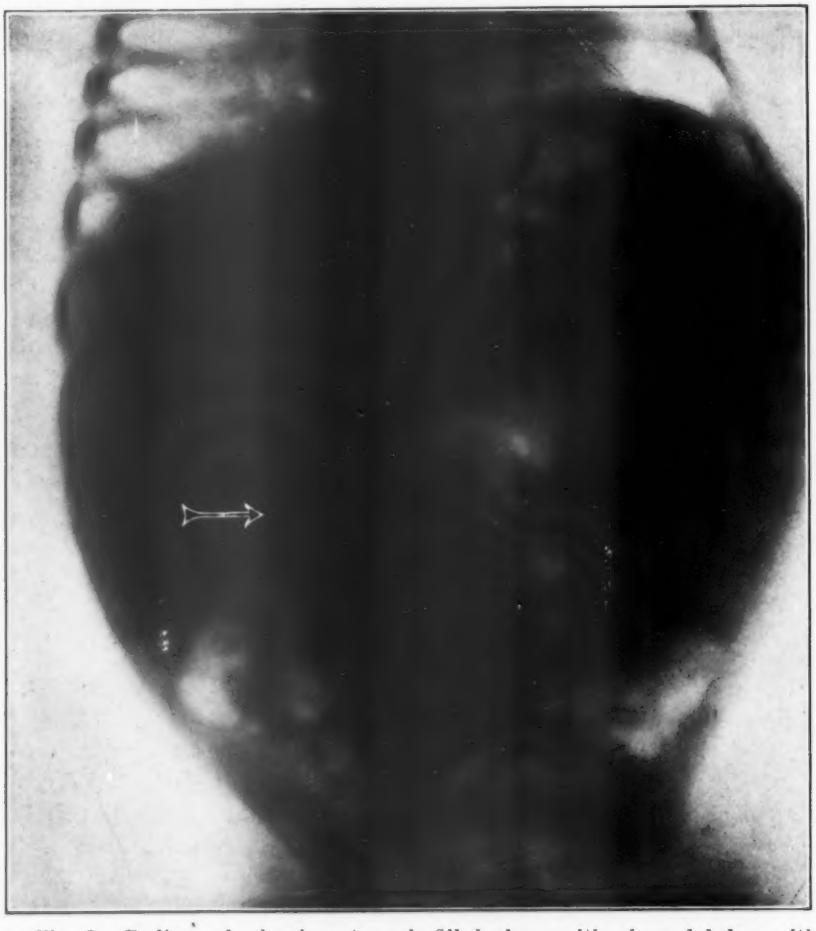

Fig. 3.—Radiograph showing stomach filled above with air and below with bismuth mixture, which has also entered the duodenum. The arrow indicates the position of the ball at the end of tube within the duodenum.

fort. Some of the older infants were constantly annoyed by it, but far more often the babies did not seem to be aware of its presence, and frequently sucked it as they do a pacifier, dozing all the while. The child, of whom I show the radiographs, fell fast asleep about ten minutes after the tube was inserted.

PURPOSES FOR WHICH THE TUBE MAY BE USED

I have remarked that the first question generally asked has been as to how we are to know that the tube is in the duodenum; the second has been as to the application of the tube. It is very difficult to state the scope of any new instrument or method. It is doubtful whether the stomach-tube seemed to be of great value when it was first suggested. I candidly admit that I cannot fully answer this question, and clearly define the value of the duodenal tube for infants. It seems to me, however, that it may well be of value in studying the physiologic or pathologic processes of digestion. Intestinal fistulas have always been prized as rare opportunities, especially in early childhood, for such investigations, and here we have a method of stimulating, to a certain extent, such a fistula. It would seem worth while, to mention merely one subject, to ascertain whether the duodenal juice containing, as it does, the various ferments of the pancreas and of the upper intestine, is the same in normal infants and in cases of marked malnutrition. This is a phase which I hope later to report on. There are many other pathologic problems which its use may help to solve; for example, the secretion of bile in icterus of the newborn; pharmaceutic problems, as for example, the excretion of drugs through the bile; or the effect of drugs on the glandular secretions; dietetic studies; for example, the influence of certain food stuffs on the quantity or quality of the ferments. These and many other investigations may be undertaken by this method.

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SPASM OF THE PYLORUS IN INFANCY

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CHRONIC GASTRIC INDIGESTION

Everyone who sees many sick infants is familiar with the symptomatology of chronic gastric indigestion at this age. It seldom occurs in the breast-fed, but develops, as a rule, after a longer or shorter period of bad artificial feeding. Vomiting is the most prominent symptom, occurs without any definite relation to the time of taking food and is never explosive. The amount of the vomitus rarely exceeds that of the food taken at the last feeding and the vomitus usually shows evidences of disturbance of the gastric digestion. The stools often present the evidences of an associated intestinal indigestion, but constipation, as the result of the reduction in the amount of food retained, is not uncommon. The stools are, however, never of the starvation type, but show by their characteristics that food is passing from the stomach into the bowel. There is never any visible peristalsis and, of course, no tumor to be felt at the pylorus.

HABITUAL VOMITING

Another not very uncommon condition is that in which a baby, without any other symptoms of indigestion, vomits habitually and yet gains steadily and appears normal in every other way. This is often, especially in the breast-fed, due simply to an excessive amount of food. In both the breast-fed and the bottle-fed, however, it is probably more often due to the imperfect closure or lack of tone of the cardiac orifice. This is shown by the facts that vomiting rarely takes place when they are quiet and that it varies with the amount of exertion and the position of the baby. The vomiting is never explosive and the vomitus shows no evidences of indigestion. There is, of course, no visible peristalsis or palpable tumor. The following case is a good example of this condition:

Anne A. was born at full term June 11, and weighed 7 pounds. She was nursed for a few weeks. She vomited a good deal but had normal movements. The milk then gave out and the child was put on a home modification of cows' milk. She continued to vomit, although various modifications, including whey mixtures, were tried. The percentages of fat had never been excessive but had never been low. None of the mixtures had been very highly alkaline. Variations in the length of the intervals and in the amount of food had made no difference in the vomiting. The vomiting occurred at any and all times, sometimes even just before a feeding. She never vomited during the night. The vomitus never contained bile. The bowels moved regularly, the stools being of good size and well digested. She was happy, active, and seemed well. She had gained regu-

larly but slowly in weight, weighing when she was seen, September 29, 10 pounds and 8 ounces. The physical examination showed nothing abnormal in any way. Variations in the composition of the food, including low percentages of fat and high alkalinity, made no difference in the vomiting, which, however, gradually diminished and finally ceased when she was a year old. At the age of nearly 3 years she was perfectly well.

SPASM OF THE PYLORUS

The symptomatology of spasm of the pylorus is materially different from that of the two conditions just mentioned, so different that the diagnosis from these conditions ought always to be possible. In the majority of instances the babies are of the excitable, irritable and neurotic type. It occurs in both the bottle-fed and the breast-fed, but more often in the former than in the latter. The symptoms seldom appear immediately after birth, but usually develop in the first few weeks, although they may not manifest themselves until the baby is some months old. The symptomatology of this condition varies considerably according to the amount of spasm present in the individual instance.

In the milder cases there is frequent vomiting, which is at times explosive and at others not. It is often preceded and accompanied by evidences of gastric pain and distress. The amount of material vomited does not ordinarily exceed that taken at the last meal. The vomitus shows, as a rule, little or no signs of disturbance of digestion. There is a tendency to constipation, but the stools show plainly that a considerable proportion of the food ingested passes through the pylorus into the intestine. The disturbance of nutrition is not extreme. The following case is a good example of this type:

Catherine D. was born February 17. She was started at once on eleven feedings of 2 ounces of a mixture of one part of whole milk and two parts of barley water. She continued to take this until March 19, when she was given ten feedings of 2½ ounces of a mixture containing 2 per cent. of fat, 5 per cent. of milk sugar, 0.75 per cent. of whey proteids and 0.25 per cent. of casein, with lime water equal to 10 per cent. of the total quantity. The child was seen March 27. She was said to have vomited after every feeding since birth. She had vomited large amounts, so that very little was retained. The vomiting had been explosive. Water was vomited the same as milk. The bowels had always been constipated.

The child was small but fairly nourished and of good color. The skin was in good condition. The anterior fontanelle was level. The posterior fontanelle and the sutures were still open. The heart and lungs were normal. The level of the abdomen was a little above that of the thorax. There was no bulging of the epigastrium. There was no visible peristalsis, even on flicking the abdomen, and no tumor was felt. The examination showed nothing else abnormal. She weighed 2,580 grams.

The stomach was washed out and found to contain considerable curdled milk and mucus. There was no visible peristalsis and no tumor was made out, even when the stomach was full of water.

She was given twelve feedings of 45 c.c. each of whey. She vomited after about half of her feedings, but the vomiting was never explosive. The amount of the vomitus varied considerably. The stools were small and green, and were composed mostly of mucus although they contained a few fine curds.

The stomach was washed out again on March 30, half an hour after a feeding. The stomach was empty, although she had not vomited more than a teaspoonful after the feeding. There was no visible peristalsis, even when cold was applied to the abdomen. No tumor was felt either when the stomach was full or when it was empty, although the abdominal walls were lax. The amount of whey was increased to 60 c.c. at each feeding.

April 2 the child was given ten feedings of 60 c.c. each of a mixture containing 1.50 per cent. of fat, 7 per cent. of milk sugar, 0.75 per cent. of whey proteids and 0.25 per cent. of casein, with lime water equal to 25 per cent. of the cream. The vomiting then increased in both frequency and amount, but the stools began to show a little fecal matter.

The amount of food was increased to 75 c.c. April 4. The application of flaxseed poultices to the epigastrium for twenty minutes before and after each feeding was begun at this time and four days later the administration of 1/80 of a minim of the tincture of opium twenty minutes before each feeding was started.

The strength of the food was gradually increased, so that on May 16, when the child was last seen, she was taking ten feedings of 90 c.c. each of a mixture containing 3 per cent. of fat, 7 per cent. of milk sugar, 0.75 per cent. of whey proteids and 0.50 per cent. of casein, with lime water equal to 25 per cent. of the milk and cream. She was vomiting a little after about half of the feedings and the vomiting was at times explosive. She was, however, having three or four stools daily, which were of fair size, greenish-yellow in color, and contained some small curds. At no time was there any visible peristalsis or tumor. She had increased in weight up to 3,040 grams.

The child was alive and well when 3½ years old.

In the more severe cases there is visible peristalsis in addition to the symptoms already mentioned as characteristic of the milder type. These symptoms are more marked than in the mild cases, the stools show less fecal residue and the disturbance of nutrition is much greater. There are numerous instances of this type on record, among which may be mentioned those of Koplik,[1] Case 2; Griffith[2]; Ibrahim,[3] Cases 4, 5 and 7; Pease[4]; Rosenstern,[5] Case 2; and Engel,[6] Cases 1 and 2. It is probable that many of the cases of Heubner,[7] Finkelstein,[8] Hutchison[9] and others, which have been reported as cases of congenital hypertrophic stenosis of the pylorus with recovery under medical treatment, belong in this class. Many of these cases show signs of motor insufficiency for a long time. The following cases are good examples of this type:

Winthrop B.[10] was born May 21, and weighed 10 pounds. His mother tried to nurse him but had practically no milk, so that at the end of two weeks he

1. Koplik: Am. Jour. Med. Sc., 1908, cxxxvi, 1.
2. Griffith: Arch. Pediat., 1905, xxii, 721.
3. Ibrahim: Die angeborene Pylorusstenose im Säuglingsalter. S. Karger, 1905; Therap. Monatsh., 1908, xxii, 560.
4. Pease: Lancet, London, 1909, ii, 1280.
5. Rosenstern: Deutsch. med. Wchnschr., 1910, xxxvi, 31.
6. Engel: Deutsch. med. Wchnschr., 1909, xxxv, 1271.
7. Heubner: Die Therapie der Gegenwart, 1906, viii, 433.
8. Finkelstein: Jahrb. f. Kinderh., 1896, xliii, 105.
9. Hutchison: Clin. Jour., 1908, xxxii, 343; Brit. Med. Jour., 1910, ii, 1021.
10. Morse: Boston Med. and Surg. Jour., 1906, clv, 343.

weighed but 9 pounds. He was then given various modifications of milk but did badly, having much colic and many bad movements, but no vomiting. He lost weight rapidly and got into such a serious condition that a wet-nurse was procured August 1, when he was 2½ months old. Her milk was, however, insufficient, so that he continued to lose weight, although his digestion was good. A variety of foods were then tried, on none of which did he do very well. Vomiting appeared first August 25. He continued to vomit and did not gain, although his stools were normal. Another wet-nurse was procured September 27. The vomiting gradually increased, nevertheless, although he continued to have good-sized, well digested stools. There was no nausea, the milk coming up in gulps without effort. The vomiting was never explosive. It usually occurred soon after nursing, but he often spit up considerable amounts just before the time for the next feeding. He was seen October 15.

The child was small and thin but his color was fair, his skin supple and his muscles strong. The level of the abdomen was the same as that of the thorax. The stomach was not enlarged to percussion. Occasional waves of contraction could be seen running over the stomach from left to right. No tumor could be made out in the region of the pylorus. The rest of the physical examination showed nothing abnormal. He weighed 11 pounds.

The breast-milk was continued, the baby being fed at three hour intervals and being given three or four teaspoonfuls of lime water at each nursing. The vomiting continued, however. It usually occurred about three, ten and twenty minutes after each nursing, but often recurred just before the next nursing. The bowels moved but once in thirty-six or forty-eight hours, but the stools were of good size and well digested. There was no visible peristalsis after November 1, and no tumor was ever found.

The vomiting gradually diminished and by the time he was a year old had entirely ceased. He gained slowly during November but after that put on weight rapidly. Breast feeding was continued until he was 14 months old, when he weighed 28 pounds and was perfectly well in every way.

He swallowed a cent when 2½ years old. It went through him in twenty-four hours. At the age of 6 years he was perfectly well.

Edwina W. was born July 8 and weighed 13 pounds. She was not nursed but was given various proprietary foods and milk modifications, none of which agreed. She began to vomit when she was only a few hours old. She did not vomit every day but would vomit frequently for several days, would then go two or three days without vomiting, and so on. She seemed perfectly normal between the attacks, took her food eagerly and retained it apparently without discomfort. She sometimes vomited what was apparently two or three times the amount of food taken at the last feeding. The vomitus was sour and contained curdled milk but no mucus. There was no relation between the time of the vomiting and that of the feeding. She vomited with some difficulty, often straining a good deal. She had frequent attacks of colic, which were not associated with vomiting, and belched much gas. She had from three to five stools a day, normal in color, amount and consistency. She had gradually lost weight; when seen, August 19, she weighed only 3,360 grams.

The child was fairly developed and nourished. The stomach reached 2 cm. below the navel. Slow peristalsis from left to right was distinctly visible. No tumor was felt. She was discharged from the hospital September 22. At that time she was vomiting but once or twice a day and sometimes went several days without vomiting. The vomiting was at times explosive, but was more often regurgitation. She at first had from three to seven small, brownish-green stools, composed largely of mucus, daily. The stools began to be yellow and to contain a few curds August 26. Early in September the stools became yellow, sufficient in amount and well digested, both macroscopically and microscopically. Peris-

talsis was at times visible up to the time she was last seen. No tumor was felt at any time. Her weight, September 22, was 3,580 grams.

The food given in this infant's case was as follows:

August 19.—Whey, twelve feedings, 2 ounces each.

August 22.—Fat, 0. per cent.; milk sugar, 7 per cent.; whey proteids, 0.90 per cent.; casein, 0.25 per cent.; lime-water equal to 20 per cent. of the milk; eight feedings, 3 ounces each.

August 25.—Fat, 0.75 per cent.; milk sugar, 7 per cent.; whey proteids, 0.90 per cent.; casein, 0.50 per cent.; lime water, 20 per cent. of the milk and cream; eight feedings, 3 ounces each.

August 27.—Fat, 1.25 per cent.; milk sugar, 7 per cent.; whey proteids, 0.90 per cent.; casein, 0.25 per cent.; lime water, 20 per cent. of the milk and cream; eight feedings, 3 ounces each.

August 30.—Fat, 1.75 per cent.; milk sugar, 7 per cent.; whey proteids, 0.90 per cent.; casein, 0.50 per cent.; lime water, 20 per cent. of the milk and cream; eight feedings, 3 ounces each.

September 14.—Fat, 2.25 per cent.; milk sugar, 7 per cent.; whey proteids, 0.90 per cent.; casein, 0.50 per cent.; lime water, 20 per cent. of the milk and cream; eight feedings, 3 ounces each.

The patient was seen again when 6½ months old. She was then perfectly well, did not vomit, and had normal movements. Her mother said that she had not seen any peristalsis for a long time. She was in very good general condition. The abdominal examination showed nothing abnormal.

Some of these infants die and no thickening of the pylorus or narrowing of its lumen is found on post-mortem examination (Cautley,[11] Carpenter[12]), thus proving beyond a doubt the existence of this condition. The majority recover under breast or careful artificial feeding and medicinal treatment. The visible peristalsis may persist for weeks or months after the cessation of the vomiting. It was noted in one of Ibrahim's patients (Case 6) for four months.

In the most severe cases there is also a palpable tumor at the pylorus (Rob[13]; Clowes[14]; Hutchison; Carpenter; Rosenstern, Cases 1, 3 and 4). This tumor is usually small in comparison with that felt in congenital hypertrophic stenosis of the pylorus. It is variously described by different authors. Koplik describes it in one of his patients (Case 3) as a "thin, cord-like structure" and later as "large as a bean," and in another (Case 1) as "soft and cord-like," while Clowes describes it as "the size of the end of the thumb." Ibrahim states that in one of his patients (Case 6) it was 3 cm. long and that it could be felt to contract and relax. In one of my patients, who is still under observation, it seems about 2 cm. long and 1 cm. thick and can be felt to contract and relax. The authors unfortunately give practically no data as to how long the tumor was palpable in these cases, merely stating that the patients recovered, leaving it to be assumed that the tumors disappeared. There are no records, as far as I am aware, of autopsies on infants in whom a tumor

11. Cautley: Brit. Jour. Child. Dis., 1908, v, 179.
12. Carpenter: Lancet, London, 1908, i, 779.
13. Rob: Lancet, London, 1906, i, 1751.
14. Clowes: Lancet, London, 1908, ii, 534.

was palpable, to show that the tumor really disappeared. Autopsies in several of the cases which have been reported as instances of this condition have, however, shown definite thickening of the pylorus (Bloch[15]; Ibrahim, Case 3; Batten[16]). This fact, of course, makes the accuracy of the diagnosis in these cases somewhat doubtful.

THE RELATION BETWEEN SPASM OF THE PYLORUS AND CONGENITAL HYPERTROPHIC STENOSIS OF THE PYLORUS

The questions immediately arise as to the relation between these cases of pyloric spasm with palpable tumor and mild cases of congenital hypertrophic stenosis of the pylorus, and the part which spasm plays in the etiology and symptomatology of congenital hypertrophic stenosis of the pylorus. It will be better, perhaps, to consider the latter questions first. There has been, and still is, much difference of opinion as to the part which spasm plays in the etiology of congenital stenosis of the pylorus, some claiming that it is the direct and sole cause of this disease; others that it has no part in its development. The weight of the evidence seems to prove, however, that stenosis of the pylorus in infancy is a congenital condition and that spasm plays no part in its causation, either before or after birth. The strongest points in favor of the congenital origin of the stenosis are the facts that the condition has been found in the fetus, that the symptoms not infrequently appear immediately after birth and that the hypertrophy is largely local.

Cautley's arguments seem to show conclusively, moreover, that spasm cannot be the cause of hypertrophy. They are in brief as follows: Spasm of the pylorus may occur at any age. It is not an affection peculiar to the first months of life. There is no proof of the development of hypertrophy of the pylorus at other ages as the result of spasm. There is no evident reason why spasm of the pylorus should cause hypertrophy in infancy when it does not at other ages. Pyloric spasm may prove fatal in infancy without causing hypertrophy. There is no analogous hypertrophy in other parts of the alimentary canal as the result of spasm. Prolonged anal spasm does not cause it. The pylorus is normally in a state of contraction. It dilates to allow the passage of the gastric contents in response to stimuli from the duodenum. It does not seem reasonable that the amount of spasm sufficient to oppose the stimulus to dilatation can be great enough to produce the excessive hypertrophy of the circular muscular fibers so constantly present. If the hypertrophy is due to spasm the longitudinal fibers should be as much hypertrophied as the circular, but they are not. Further evidence that the hypertrophy is not due to spasm is that the hypertrophy does not disappear after gastro-enterostomy

15. Bloch: Jahrb. f. Kinderh., 1907, lxv, 337.
16. Batten: Lancet, London, 1899, ii, 1511.

(Morse, Murphy and Wolbach[17]). It is evident, therefore, that primary pyloric spasm and congenital stenosis of the pylorus are two independent conditions.

Although pyloric spasm and congenital hypertrophic stenosis of the pylorus are unquestionably distinct entities, there is no doubt that spasm plays an important part in the production of the symptoms in many cases of pyloric hypertrophy. In this way only can the sudden onset of the symptoms be explained in many instances in which marked hypertrophy is found at operation. The following case is an example of this type:

Arthur H. was seen when five weeks old. He was born two weeks before he was expected and weighed 4 pounds and 14 ounces. He was breast-fed from the start and had been perfectly well except for a considerable amount of colic. He had not vomited and the stools had been normal until September 7, four days before he was seen. He had gained 1½ pounds.

The mother began to menstruate September 7. The baby vomited at once. The first vomitus contained a little bile. His stool that morning was of good size and well digested. The nursing was stopped and he was given water only. He was also given some castor oil. He retained the castor oil but vomited the water.

He was given nothing except a little brandy and water on the eighth and did not vomit. The nursing was begun again on the ninth. He was given a little water before the nursing and the duration of the nursing was limited to 2½ minutes. He began to vomit again after seven or eight hours.

September 10 he was given one ounce every 1½ hours of a mixture of 1 ounce of skimmed milk, 1½ ounces of lime water and 8 ounces of water. The vomiting persisted and the amount was reduced to half an ounce at a feeding. This was also vomited, so that for the twenty-four hours before he was seen, September 11, nothing at all had been retained. The bowels had been moved by enemata. The stools had consisted of green mucus. The vomiting had been projectile.

The child was small and thin but in fair condition. His color was good. The examination showed nothing abnormal except in the abdomen. The ingestion of half an ounce of water was followed by marked visible gastric peristalsis, running from left to right. A tumor, the size of a small marble and moderately movable, was felt in the region of the pylorus. A stool, which was seen, was small, loose, greenish-brown in color and composed almost entirely of mucus.

Gastro-enterostomy was done the same day by Dr. C. L. Scudder, who found a tumor at the pylorus the size of the last phalanx of the thumb. He has done uninterruptedly well since the operation, five months ago.

In many cases of slight or partial stenosis of the pylorus, the symptoms in considerable part are undoubtedly due to the spasm. When the spasm is relieved by appropriate treatment the symptoms diminish and in mild cases disappear. A large proportion of the reported cures by medical treatment of cases of pyloric stenosis in which distinct tumors have been felt are undoubtedly to be explained in this way (Batten; Bloch; Ibrahim, Case 3; Rosenstern, Cases 1, 2 and 3; Finkelstein; Heubner, et al.). In fact, no other explanation seems possible, because the evidence at autopsy in "recovered" cases (Ibrahim, Case 3; Batten; Bloch) shows that the hypertrophy remains many months, at least, after

17. Morse, Murphy and Wolbach: Boston Med. and Surg. Jour., 1908, clviii, 480.

the cessation of symptoms. There is, as far as I am aware, no data based on operative or post-mortem findings, as to the anatomic conditions in these cases years after the relief of symptoms. It is probable, however, that a certain number of the cases of benign pyloric obstruction which develop in the third and fourth decades are the final results of mild cases of congenital pyloric stenosis. Many of these patients also show evidences of motor insufficiency years after the cessation of symptoms (Bernheim-Karrer[18]).

DIAGNOSIS BETWEEN SPASM OF THE PYLORUS AND CONGENITAL HYPERTROPHIC STENOSIS

While there is no question that spasm of the pylorus and congenital hypertrophic stenosis of the pylorus are two distinct conditions, the diagnosis between them is at times an extremely difficult one. The onset of the symptoms is the same in both, the vomiting is explosive in both and there is visible peristalsis in both. Constipation and loss of weight are common to both. There is sometimes a palpable tumor in spasm; the tumor is sometimes not palpable in hypertrophic stenosis. In spite of the similarity of the symptoms of the two diseases there should be little difficulty in distinguishing the marked cases of hypertrophic stenosis from those of spasm, because the constipation is never so marked or persistent in spasm as in stenosis and because the tumor in spasm is small and cord-like, not large and hard as in hypertrophic stenosis. Variation in the size of the tumor during examination is practically positive proof that the condition is one of spasm, not of hypertrophy. The difficulty in diagnosis comes between the severe cases of spasm and the mild cases of hypertrophic stenosis, because the difference in the symptomatology of the two diseases is entirely in the degree, not in the kind, of symptoms.

In many instances it is impossible at first to make a positive diagnosis between these two conditions. If the baby is breast-fed the chances are much in favor of hypertrophic stenosis, because spasm is very unusual in the breast-fed while hypertrophic stenosis is equally common in the breast-fed and in the artificially fed. If the baby is artificially fed the chances are even, although if the feeding has been very irrational, spasm is a little the more probable. The absence of a palpable tumor is strong evidence against hypertrophic stenosis but does not positively exclude it, because a good sized tumor has sometimes been found at operation when none was felt before it. It is never safe to conclude that there is no tumor, however, unless the abdomen has been examined with the stomach both full and empty and with the abdominal walls relaxed, if necessary under an anesthetic. If no tumor is felt under these conditions an almost posi-

18. Bernheim-Karrer: Jahrb. f. Kinderh., 1909, lxix, 551.

tive diagnosis of spasm is justified. Examination of the gastric contents is of little or no assistance, because there are very few reliable data as to the chemistry of the gastric contents in these conditions and what few data there are are contradictory. An excessive hyperacidity perhaps counts a little, however, in favor of spasm. Dilatation of the stomach seldom develops in simple spasm of the pylorus and, if it does, is always slight. It develops in a certain proportion of the cases of hypertrophic stenosis but is seldom extreme. The presence of dilatation is, therefore, in favor of hypertrophic stenosis and against spasm. Its absence does not, however, count at all in favor of spasm. Dilatation of the stomach, unless extreme, is very difficult of demonstration in infancy. Too much importance must not be attached, therefore, to what are apparently slight degrees of dilatation. Rapid improvement under medical treatment and regulation of the diet is strong evidence in favor of spasm, but does not positively exclude a mild degree of hypertrophic stenosis complicated by spasm. The most important points in favor of spasm in doubtful cases are, therefore, the absence of a palpable tumor, or, if a tumor is present, its cord-like feel, the presence of intermittent contraction and relaxation of the tumor, and rapid improvement under medical treatment and regulation of the diet.

ETIOLOGY

The etiology of spasm of the pylorus in infancy is very obscure. It is apparently most common in excitable and irritable infants, the offspring of neurotic parents. Some writers believe that the normal muscular hyperirritability at this age predisposes the pylorus to spasm. The mechanical irritation of the food or the chemical products of digestion thus directly or reflexly cause spasm when they would not in later life. Others believe that disturbance of the gastric digestion always precedes and causes the spasm. Some observers have found a hyperacidity of the gastric contents, others have not. Engel believes that a gastrosuccorrhea is at the bottom of the trouble. It is safe to conclude, at any rate, in view of the conflicting opinions and the insufficiency of the data, that nothing is known as to the etiology which is sufficiently reliable to serve as a basis for treatment.

TREATMENT

The most important part of the treatment of pyloric spasm is regulation of the diet. The best food is good breast-milk. If this is vomited, it is well to remove a part of the cream and add lime water. The next best food is some modification of cow's milk. It is advisable to keep the percentage of fat low, because fat tends to delay the emptying of the stomach. It is also advisable to give as large a proportion as possible of the proteids in the form of whey proteids, because they are not coagu-

lated by rennin and easily pass the pylorus. An alkali should be added to the milk to neutralize any possible hyperacidity and to delay the coagulation of the casein by rennin and thus favor the passage of the liquid milk through the pylorus. These general principles serve, of course, only as a basis for the preparation of the food, which must be varied to suit the individual baby. Plain whey is very useful in some instances; so also is pancreatization in others.

There is much difference of opinion as to whether the food should be given at short or long intervals and as to the quantity which should be given at a feeding. The most rational way of regulating the interval between feedings is to determine how long it takes the stomach to empty itself in the individual case and to make the interval somewhat longer than this. In general, it is probably better to give small amounts at a feeding, although there are many exceptions to this rule.

Daily lavage with plain water or a weak solution of bicarbonate of soda is of assistance in most cases, although some authors think that it tends to keep up the spasm. Warm applications to the epigastrium are sometimes of assistance. Minute doses of some preparation of opium—for example, 1/40 of a minim of the tincture—given a short time before feeding, sometimes seem to diminish the spasm. Atropin and cocain have also been used for the same purpose. It is also important to keep these babies very quiet, especially immediately after feeding.

Rosenhaupt[19] claims good results in this condition from rectal irrigations of salt solution, basing his treatment on Engel's statement that the cause of the trouble is gastrosuccorrhea, and on Benczur's experiments which show that in animals rectal injections of salt solution diminish the secretion of gastric juice. He obtained favorable results in all but one case, but does not state how many patients he treated. Rosenstern claims good results in four cases from the rectal instillation of from 250 c.c. to 400 c.c. of Ringer's solution daily. This method of treatment is, however, so new that it must be regarded as still *sub judice*.

Surgical intervention for the relief of pyloric spasm is seldom either necessary or advisable. Carpenter compares it to tracheotomy for laryngismus stridulus. This comparison is, however, perhaps a little too strong, because experience has shown that babies sometimes die of this condition under medical treatment. Surgical intervention is, therefore, justified in certain extreme cases. An exploratory laparotomy certainly ought to be done in all cases in which there is a reasonable doubt as to whether the condition really is one of spasm and not of hypertrophic stenosis and in which the patients are doing badly under medical treatment.

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19. Rosenhaupt: Deutsch. med. Wchnschr., 1909, xxxv, 1789.

BLOOD TRANSFUSION IN INFANTS BY MEANS OF GLASS TUBES*

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The value of transfusion in infants has been demonstrated in the treatment of hemorrhagic disease of the new-born and in cases of hemorrhage after injuries or operations. That this procedure has not been more frequently and successfully tried in these conditions is probably due to the technical difficulties of the operation in infants, and especially in the new-born infant. The chief difficulty is found in uniting the artery of the donor to the small and inaccessible vein of the infant. The largest superficial veins of a baby's arm are so small that one must resort to the less accessible veins of the thigh which, at the best, are scarcely large enough. However, when once a satisfactory connection is made between artery and vein, a flow of comparatively short duration is sufficient to transfer enough blood for an infant. In a baby weighing 8 pounds, a flow of five minutes corresponds to thirty or forty minutes in an adult.

The ordinary methods of transfusion are adapted to the requirements of adults and cannot be so successfully applied to infants. Babies have been transfused by the method of direct suture and with the Crile and Elsberg cannula, by men experienced in this kind of work. Less skilful operators using these methods sometimes find it impossible to transfuse a small infant. The unsuccessful attempts result from a failure to start the flow of blood rather than an inability to maintain it for a sufficient length of time.

Under these circumstances it seems more practical to use a method on infants which will lessen the mechanical difficulties of connecting the vessels, even if, in a technical sense, it is not so perfect as the ordinary methods in present use.

It occurred to me that the use of coated glass tubes, as suggested by Brewer in 1909, might simplify this problem. With this end in view, I conducted a series of laboratory experiments to determine how this method might be modified to suit the needs of infants.

The results, and not the details, of these experiments will be given in this paper. I wish more particularly to describe in detail the prep-

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*From the Laboratory of Surgical Research, Harvard University Medical School. Read at the fourteenth meeting of the New England Pediatric Society, Boston, Feb. 25, 1911.

aration and use of these tubes in transfusing infants, and to report three cases which will illustrate their practical application.

Some of the experiments were made on dogs, but most of the work was done with cats, because their small and delicate vessels more nearly resemble those of the infant.

EXPERIMENTAL WORK

The usual experiment consisted in first bleeding an animal and then reviving it by transfusion, using glass tubes in various lengths and sizes. The common carotid artery of the donor was joined to the recipient's external jugular vein, or one of its smaller branches. In some cases the femoral vessels were used.

The tubes were made from glass tubing of the smallest sizes, cut into lengths varying from 3 to 8 cm. The ends of these tubes were pointed, and all sharp edges smoothed away in the flame. About 3 mm. from either end the tubes were encircled by a shallow groove. This carried the ligature, with which the vessel was tied over the end of the tube.

Straight tubes proved to be better than curved tubes. They are easier to handle and the blood does not clot so quickly in them. The tendency of the blood to clot was found to increase as the tubes were lengthened and their diameters diminished, but a flow of at least ten minutes could always be obtained with tubes 8 cm. in length and 3 mm. in diameter.

Various materials for lubricating or coating the tubes were tried, such as liquid petrolatum, vaselin, stearin, and paraffin, as suggested by Brewer. Vaselin gives too soft a covering and stearin alone is too hard and rough. Paraffin, 54°, is easy to handle and gives a fairly firm, although rather uneven coating. A mixture of vaselin, paraffin and stearin in 2-2-1 proportions gave the smoothest, hardest covering. Blood ran longer without clotting in tubes coated with this mixture than in those coated with paraffin alone. Of any one material, paraffin was by far the most satisfactory. In the course of the experiments, it was found that blood ran surprisingly well in plain glass tubes, and I am sure that they could be used with a fair chance of success if the coated tubes were not available.

The practice gained in working out the technical details in the laboratory was of great value in performing the actual operation on infants.

TECHNIC

The instruments required in the operation are those of an ordinary dissecting layout, to which are added fine scissors, two pairs of small forceps, at least three mosquito hemostats, and the three small tenacula which come with the Elsberg transfusion cannula.

These fine hooks are indispensable in exposing the lumen of the vein until it has been dilated and the tube inserted. Crile clamps can be used to control temporarily the donor's artery, but a small, light artery clip is needed for the infant's vein.

The tubes can be freshly prepared in a few minutes before each operation. The mixture of vaselin, paraffin and stearin, which looks like wax and might be conveniently so designated, is kept in a glass dish, or better a metal box. I use a shallow box 5 inches long and 2 inches wide. Its cover, when turned up, serves as a handle.

It is well to prepare one or two extra tubes for each transfusion. The dry tubes are placed in the box with the mixture, and sterilized by heating over any convenient flame. The tubes fill by capillary attraction as they sink into the melted wax. One is then taken from the box with a sterile hemostat which grasps it near the middle. By slowly tipping the tube the wax is made to run from end to end until it covers every surface. The excess is then drawn off by touching the end of the tube with sterile cotton or gauze, which quickly absorbs the melted wax. I have found this easier and more certain than the method of shaking the wax out of the tube. The wax adhering to the tube hardens in a few seconds into a smooth, firm coating which is not damaged by careful handling during the operation. Tubes not perfectly coated are dropped back into the box, reheated and treated as before.

In many of the laboratory experiments, the small amount of air which a tube contains was forced into the recipient's circulation ahead of the donor's blood. Although no evil effects were noted, it is safer to eliminate all danger of air embolism by filling the tubes with salt solution. This can be done with a small glass or soft rubber syringe. A convenient substitute for the syringe is a piece of cotton or gauze saturated with salt solution. The salt solution can be squeezed from this into the tube and held there by placing in one end a plug of sterile cotton covered with vaselin. This plug is removed after the tube has been tied into the infant's vein and just before it is connected with the donor's artery.

About 2 inches of the donor's radial artery is isolated in the usual manner under cocain. The infant is lightly anesthetized and the femoral, the popliteal, or the long saphenous vein is exposed in the thigh. In the cases here reported, the saphenous vein was not readily found, and the dissection was at once carried down to the femoral vein. This vein is of fair size but rather awkwardly placed on account of its depth. If possible, at least an inch of the vein should be freed. It is then clamped above and tied below. The ligature is left long to act as a guide. The vein is partly cut through just above the ligature and two of the small tenacula are hooked into the edges of the cross slit. The vessel is then completely divided and the third hook so placed as to expose its lumen.

It is important to keep control of the vessel with the hooks in this way, for the lumen is very hard to find if such a delicate vein is allowed to collapse.

The vein is gently dilated with a small hemostat. An infant's vein is fortunately much tougher than a cat's, and a very small vessel can be dilated to a useful size. After washing out the vein with salt solution, the tube, lubricated with vaselin, is inserted and secured with a fine silk ligature.

The donor's artery is clamped, divided and tied over the other end of the tube. One should make certain that the vein is not twisted before the tube is tied into the artery. When the clamp on the artery is removed, the stream of blood is seen to start through the glass tube, but its continued flow can only be verified by the pulsations in the vein and the appearance of the child. An infant is very quickly filled with blood from an adult's radial, and careful watch should be kept of the baby's face to see that the blood is not transfused too rapidly or in too great an amount. In the second case here reported, the child's face became a little dusky at the end of five minutes but regained a normal, red color a few minutes after the transfusion was finished.

CASE REPORTS

CASE 1.—The first case, one of hemorrhage after a minor operation, was transfused by this method before the laboratory experiments had been completed. William L., an infant aged 6 months, weighing 11 pounds, entered the Boston Floating Hospital July 10, 1910, on account of intestinal indigestion. The next day an indurated mass was noticed in the child's right cheek. During the following twenty-four hours the induration increased and an ulcerated area appeared on the buccal surface of the cheek. July 13, an incision was made into the cheek but no pus was found. After the operation, there was a small but persistent hemorrhage from the wound which continued throughout the night. Several dressings were soaked with blood. In the morning the bleeding not having checked, the child was sent to the Boston Children's Hospital. As far as could be learned, the baby had never bled in this way before, nor was there any suggestion of hemophilia in the family history.

When examined in the Children's Hospital, the child was still losing a little thin, watery blood from a 2-inch incision in the right cheek. The wound was sutured and the oozing stopped. The infant, however, was in poor condition. The skin, lips, and fingers were blanched. The respirations were rapid and shallow, and the pulse, though perceptible, could not be counted at the wrist. The hands and feet were cold. The child was semi-conscious. Preparations were at once made for transfusion. Unfortunately, in the hurry, the hemoglobin and coagulation time were not determined.

The mother, a small woman, served as donor. Her right radial artery was exposed under cocain. The vessel proved to be unusually small. It scarcely seemed half the normal size. The child required little ether. An incision was made over the long saphenous vein at about the middle of the right thigh. The superficial vein not being found after a short search, the dissection was carried down to the femoral vein above Hunter's canal. The vessel was isolated for about an inch of its length and connected with the donor's artery by means of a coated glass tube, in the manner already described. In this case the tube was not filled with salt solution, but the air which passed into the infant's circulation

apparently did no harm. The tube was 6 cm. in length and 2.5 mm. in diameter. The flow of blood lasted for about seven minutes. When disconnected at the end of ten minutes, the tube was filled with a clot. In that time the child's color had greatly improved. Lips, ears and fingers showed a red tinge. The breathing was slower and deeper and the pulse stronger and fuller at the wrist. After ligating the femoral vein the lower leg became swollen and slightly blue. This passed away in a few hours. One hour after the operation, the child's pulse had fallen to 140. The improved condition, which immediately followed the operation, was maintained during the day and succeeding night. From this point the convalescence was uneventful and the infant was referred back to the Floating Hospital ten days after the transfusion.

CASE 2.—The second case was one of hemorrhagic disease of the new-born. James S., was referred to the Infant's Hospital in Boston by Dr. Homan of Everett, Mass., Oct. 11, 1910. The child, born two days before, at full term, normal delivery, was perfectly well up to 1 a. m. on the day of entrance, when he began to vomit blood in large clots. He vomited frequently and spat up bright, red blood after each feeding. During the day he had three movements containing red blood. He was brought to the hospital at 4 p. m.

The child weighed 6½ pounds. The skin was slightly jaundiced and very pale. There was still a trace of color in the lips. About the mouth and anus, the skin was stained with fresh blood. There were several small points of subcutaneous hemorrhages on the upper lip and in the groin. Heart, lungs and abdomen were negative. The umbilical cord was normal. The pulse could be felt at the wrist, but was too rapid to count accurately.

The infant had evidently lost considerable blood, enough to seriously affect his condition, and was in a poor state to resist any further hemorrhage. For this reason it seemed best not to temporize with the less radical measures, but to proceed, as soon as possible, with a transfusion which would stop the bleeding and, at the same time, restore the cellular elements of the blood. The father of the child served as donor. While awaiting his arrival, and preparing for the operation, the infant vomited blood twice and passed another bloody stool.

The father's left radial artery was exposed under cocain in the usual manner. The child was then given a little ether and its femoral vein isolated for about one inch in the middle of the thigh. The vein was collapsed, and, in this state, seemed scarcely more than one millimeter in diameter. Considerable difficulty was experienced in exposing the lumen of such a small vein, but once the three hooks were in place, it was possible to dilate it enough to admit the tube. Following the technic already described, the vessels of the donor and recipient were connected with a coated glass tube 8 cm. long and 3 mm. in diameter. In this case the entrance of air was obviated by using a tube filled with salt solution. The blood had been flowing for about one minute when, by some mischance, the tube was pulled from the father's artery. Before it could be replaced, the blood had clotted in its lumen. The extra tube which had been prepared was then substituted and the blood allowed to flow for four minutes. The infant rapidly took on a healthy, red color. The face was becoming a trifle dusky when the transfusion was brought to an end. Counting the time the first tube was in use, the total flow must have been of about five minutes' duration.

The next day the patient was to all appearances a normal, healthy baby. There was no more bleeding. He vomited once after the first whey feeding. During the day he passed two dark movements. Three days after the transfusion the wound was clean and the infant was sent home to be nursed by the mother. A month later he was reported in perfect health.

CASE 3.—The third case was referred to the Infant's Hospital for hemorrhagic disease of the new-born Feb. 18, 1911. Chester P. was born four days before entrance, and for the first two days appeared to be a normal, healthy baby. On the third day he did not seem so well and passed a movement containing dark blood. The next day the baby had six black movements consisting, for the most

part, of clotted blood. He vomited once but the vomitus contained no blood. The bleeding from the bowel continued until the infant became too weak to nurse, and he had lost his healthy color when brought to the hospital at 1:30 p. m. on the fifth day.

When examined at 4 p. m. he was pale but not blanched. There was some color in the lips and fingers. He had a strong cry. Heart and lungs were negative. An odor from the umbilical dressing could be easily detected. The cord was moist and sloughing, but there was no redness or induration in the skin about the umbilicus. The temperature was subnormal. The pulse was 150 at the wrist, and the respirations were regular and not rapid. The hemoglobin was 35 per cent.

At 5 p. m. the baby had a large, dark movement with a suggestion of red color. At 6 p. m. there was another dark movement but no fresh blood. At 9 p. m. he had a small, dark movement with a little fresh blood.

The baby was given 10 c.c. of a thrombin solution, prepared by Dr. W. P. Lucas, at 11 p. m., and this was repeated twice the next morning. During the night the infant had a normal fecal movement but at 8 a. m. he passed another dark stool containing a little fresh blood. The morning temperature was 101.8 F.

At this time the baby's condition seemed as good or better than the day before, and it was decided to postpone transfusion, with the understanding that it should be done in the evening for any more bleeding, even if the infant's condition had not become worse.

The baby showed no change up to 1:30 p. m. when there was a sudden collapse. He lost all his color, the breathing became labored and the pulse was imperceptible at the wrist; hands and feet were cold. He passed a small movement of fresh blood. The father was summoned at once to serve as donor.

The operation began at 2:30 p. m. The father's left radial artery was exposed under cocain. The baby needed almost no ether. His femoral vein was isolated in the left thigh. The subcutaneous tissues were exsanguinated and the little blood which escaped from the deeper vessels was thin and watery. The coated tube used in this case was 12 cm. long and 3 mm. in diameter and this extra length made it easier to complete the connection with the donor's artery.

The father had a strong pulse and large radial, and the baby was filled with blood very rapidly. The connection was maintained for four minutes, and during this period the flow was checked three times, for a few seconds, when the infant's face became a little dusky. At the end of the operation the child began to struggle and cry vigorously. The hemoglobin, taken immediately after the transfusion, was 90 per cent.

The baby slept well during the night. He regurgitated his feeding once and had one dark movement. There was no sign of fresh bleeding. In the morning the temperature was 99.8 F. During the day he had two more dark movements. The second day after the operation the temperature was normal and the baby passed a normal, yellow movement. One week after the transfusion, the infant was taking his feedings well. He had a good color and normal temperature.

295 Beacon Street.

PROGRESS IN PEDIATRICS

BACTERIOLOGY AND PATHOLOGY

Allergy

(C. E. von Pirquet: Arch. Int. Med., vii, 259)

"Allergy" is explained by von Pirquet as being the altered reaction of an organism, which has passed through a certain disease or intoxication, to subsequent attacks of the same bacteria or toxins; that is, a reaction which differs from the reaction to the first attack in time, quantity or quality. As a simple example, he cites the phenomena shown by a person when revaccinated, in distinction to the train of symptoms following a first vaccination. In the latter case, after an incubation period of eight or nine days, a papule forms which increases and goes through the stages of vesicle, pustule, crust and scar; while in the case of a revaccination a papule forms within twenty-four hours, and then soon subsides. Here there is a second reaction which differs as to time, quantity and quality from the first reaction and is a typical example of allergy.

Included within the term allergy also are the reaction after vaccination in the cutaneous tuberculin test of von Pirquet, and the local and general reactions after the subcutaneous injection of toxins (for example tuberculin), amounting in some cases to the very severe general reaction, collapse and death known as evidences of "anaphylaxis." Von Pirquet thus tabulates the divisions of allergy:

I. Altered reactivity according to time, compared to a first reaction after eight to twelve days. 1. Early reaction (immediate) within twenty-four hours. This can be obtained by: (a) Intravenous injection associated with general symptoms (death); (b) subcutaneous injection; here we have to distinguish: (1) General symptoms (fever, exanthema), (2) local symptoms (*Stichreaktion*), (3) co-reaction of other foci; (c) cutaneous vaccination; (d) conjunctival application. 2. Torpid early reaction—second to fourth day. 3. Accelerated reaction —fourth to seventh day.

II. Altered reactivity according to quantity. 1. Re-enforced reactivity (hypersensibility, a paradoxical reaction, anaphylaxis). 2. Lessened reactivity (hypersensibility). 3. Abolished reactivity (immunity).

III. Reactivity altered according to quality (changes regarding color, microscopic observations, etc.).

In this article he attempts to review all the evidences of allergy so far observed in all the different diseases and intoxications.

1. Serum Disease: The normal symptoms of "serum disease," arising after the injection of certain sera, as horse serum, in diphtheria antitoxin, are these: after an incubation period of eight to twelve days there occur fever, urticaria and joint pains. On a second injection allergic phenomena are very common; there is often an immediate reaction, that is within twenty-four hours or less; this may be local or may be very severe or even fatal in cases of anaphylaxis. There is then a change in the reaction as to time, quantity and quality. The phenomena in experimental serum disease in animals, are:

(1) Almost universal anaphylaxis caused by some sera in animals of another species—as horse serum in guinea-pigs. (2) Lessened susceptibility or anergy, or antianaphylaxis. (3) Specificity of serum allergy. (4) Passive anaphylaxis —that is, the transmission by the serum of allergic animals of the same susceptibility to another animal. (5) Transmission of allergy to offspring through the mother, not through the father. (6) Active allergy in the newly born, that is, the inability to cause anaphylaxis in newly born animals, which is parallel to the observed fact that serum disease is rare in human nurslings.

2. The injection of other albuminous substances, such as hemoglobin, egg albumin, extract of peas, etc., also give evidences of allergy; in especial, anaphylaxis has been noticed in connection with all these substances.

3. Urticaria and hay-fever, von Pirquet believes, are examples of allergy to specific toxins.

4. Vaccinia: The evidences of allergy in regard to revaccination have already been recounted.

5. In glanders, actinomycosis, lepra, diphtheria and the diseases caused by hyphomycetes, evidences of the different varieties of allergy are recorded.

6. In syphilis there is no present evidence of allergy, but von Pirquet believes that it is possible that as soon as a pure culture of the specific organism can be procured and the toxin extracted, that local allergic phenomena can be elicited; i. e., that a cutaneous test can be elicited similar to that for tuberculosis.

7. Tuberculosis is the disease in which allergy has been most widely studied on account of the diagnostic importance of the changed reactions. Von Pirquet reviews the different forms of allergy observed in tuberculosis:

1. The general reaction on subcutaneous or intravenous injection of tuberculin in tuberculous patients. If the dose is large enough the symptoms may be fatal. If the dose is smaller general symptoms of malaise and fever are present; also there is the focus reaction or the inflammatory symptoms in the neighborhood of tuberculous tissue.

2. Subcutaneous reaction or *Stichreaktion;* that is, a subcutaneous inflammation at the site of injection. This, he says, has been proved to be the most delicate test of allergy, and is generally positive in tuberculous children with doses of .10 mg. of tuberculin or less.

3. Local reactions; as, 1. Cutaneous reaction on vaccination (von Pirquet), which he says is not delicate. 2. Morro's percutaneous reaction. 3. Application to the mucous membranes, as to the conjunctiva in Calmette's reaction; or to the nasal mucous membrane.

The time necessary between the first infection and the development of allergy in tuberculosis von Pirquet thinks is one to three months.

A lessened susceptibility of tubercular individuals to tuberculin or "anergy" occurs, (1) in the first stage of infection, often in nurslings; in them the antibody has not had time to develop; (2) in the final stage of miliary tuberculosis; (3) in cachexia; (4) during measles; (5) during continued treatment with tuberculin; (6) a long time after the onset of tuberculosis; (7) in certain cases of idiosyncracy.

In the discussion as to the cause of the phenomena of allergy von Pirquet says that he early observed an incongruity between them and the generally accepted theories as to the incubation period of disease. It was formerly taught that the incubation period in an infectious disease is due to the length of time necessary for the development of the microorganisms. On this basis how can the immediate reaction taking place on a second entrance of the organisms or their toxins be explained, he asks. The theory of von Pirquet is as follows: After the introduction into the organism of bacteria or toxins the body forms certain substances called antibodies, the time necessary for the development of which corresponds to the incubation period of the disease; these antibodies then combine with the products of the infecting agent, or with the toxin, in a biochemical reaction, the result of which is another toxin which is the direct cause of the symptoms of the disease, such as fever, exanthema, etc. In diseases such as variola, measles and chicken-pox, all having a similar incubation period, he believes the exanthem is not caused by the specific microorganism, but by the toxic digestion product produced by the interaction of the antibody with some product of the microorganism. If the bacteria or toxins are introduced again within a limited time, the antibody is still present, the reaction is immediate, the toxic substance results and the symptoms of allergy occur.

G. L. Meigs.

METABOLISM AND NUTRITION

The Body of the Cretin

(A. Flinker: Wien. klin. Wchnschr., 1911, xxiv, 6, p. 196)

Flinker compares the body of a cretin with that of a normal man of the same age and concludes that the cretin has a relatively large head, short neck, long trunk and very short legs, conditions also found during childhood. Development in the cretin has evidently progressed only as far as ordinarily occurs in children, which condition has been confirmed by many pathologic examinations.

MAURICE OSTHEIMER.

Infant Mortality

(S. W. Newmayer: Pediatrics, xxiii, No. 2)

Among other points Newmayer brings out the value of individual feeding according to the infant and not according to age, as shown by the history of a large institution for children in Philadelphia. In 1909, this institution fed all the infants, according to age, on a series of set formulas of milk mixtures, and the children were cared for by nursery maids. In June, 1909, this institution, based on the number of sick children, had about 65 per cent. of deaths, in July, 1909, about 55 per cent., and a similar death-rate for August. In 1910, the managers employed a physician who was well trained in diseases of children and infant feeding; they also substituted trained nurses for the nursery help. Each child was carefully examined and watched and fed according to the physician's advice. The results were, for June, 1910, 14 per cent. mortality; July 8 per cent., and for August but 4.4 per cent.

HENRY F. KEEVER.

Calcium Metabolism in a Case of Infantile Tetany

(H. D. Haskins and H. J. Gerstenberger, Jour. Exper. Med., xiii, No. 3)

The authors report their experiments on calcium metabolism in an infant of 14 months suffering from tetany. Their observations embrace two periods, the first during the stage of active symptoms, covering a period of about six weeks; the second during the latent stage, covering one week. A table is given recording the amount of calcium in the food, the amount of calcium lactate administered, and the amount excreted in the urine and feces. Calcium lactate was given during only three weeks of the first period. The diet during the first series of experiments consisted of 100 c.c. of milk diluted with 100 c.c. of water; during the second series 1,000 c.c. of milk daily. Their results were as follows: the urinary calcium was slightly increased while calcium lactate was administered; calcium administration did not increase calcium retention; and there was no improvement in the symptoms during the administration of calcium lactate.

F. H. BARTLETT.

Should Eclamptic Mothers Nurse Their New-Born?

(J. R. Goodall: Arch. Pediat., January, 1911, xxviii, No. 1)

Goodall, discussing the question from the standpoint of the child's interests, cites three instances occurring in his practice of babies dying without apparent cause in a few hours after the first appearance of milk in the mothers' breasts. The symptoms and manner of death in all three were identical—general depression, going into coma, cyanosis, convulsions, respiratory paralysis, slow, full pulse, and abdominal distention. The mothers were eclamptic, the children apparently normal at birth. The onset of the above symptoms followed in a few hours the first ingestion of the mothers' milk. Somewhat detailed reference is made to the literature on the subject to prove that the child of an eclamptic mother is never healthy at birth and that the lesions are identical with those of the mother. These children come into the world with their organs

generally diseased, especially the kidneys. Observations by Dienst are quoted as showing that all children born of eclamptic mothers give evidences of hepatic or renal lesions to a varying extent. The author considers maternal eclampsia a frequent source of chronic nephritis in young children, believing that the milk is more toxic than either the blood or urine, and that this toxicity varies with the persistence or non-persistence of the toxemia up to the time of the filling of the breasts with milk. He concludes that in toxic and jaundiced women maternal feeding should be delayed until the condition has been controlled, and that the persistence of albuminuria makes permanent artificial feeding necessary.

F. C. Z.

ACUTE INFECTIOUS DISEASES

Some of the Rarer Occurrences in the Rheumatism of Children

(F. J. Poynton: Brit. Med. Jour., January 7, 1911)

Rashes. In an observation of 600 cases, Poynton saw forty rashes. They are usually urticarias and erythemata which may be mistaken for scarlet fever or ringworm. Psoriasis may alternate with chorea; this occurred four times in Poynton's series. Purpura and, rarely, a pemphigoid or bullous eruption may be observed. Finally, herpes has been observed independent of arsenic administration.

Erythema nodosum was observed fourteen times and it is asserted by Poynton that it is possibly not a manifestation of rheumatism, for heart disease is an unusual complication.

Venous thrombosis of the large veins in severe cases occurred five times. Localized edema, with subsequent discovery of the thrombosed veins, are diagnostic. Facial edema is occasionally caused in this way.

Tachycardia may be paroxysmal in onset and character. It is associated with mitral stenosis more frequently than with other lesions. It may precede the evident valvular lesion. In some of these cases the recovery is complete. If mitral stenosis develops, however, the tendency is for a rapid heart action to persist. As a rule Poynton has found no involvement of the thyroid and none of his cases have developed exophthalmic goiter.

Mastitis, as evidenced by slight enlargement and tenderness of the breasts in girls, was also observed by Still.

Epistaxis has been observed at the onset, during the illness or during the quiescent period. Hematemesis has been observed with grave heart disease.

J. G. M. Bullowa.

Serum Treatment of Pneumonia in Children

(E. M. Sill: Med. Rec., New York, 1911, lxxix, 712)

About a year ago Sill became interested in a polyvalent, composite serum obtained from diphtheria-immune horses, for use in pneumonia. The serum was injected subcutaneously in doses of 10 c.c., at varying intervals, depending on the symptoms and the effect it had on the patient. In some cases one injection seemed to be sufficient to relieve the symptoms and check the disease, while in others repeated injections of 10 c.c. were given every day or at longer intervals, although not always with favorable results. Sill thinks that perhaps, in these latter cases, if large doses had been given or the serum had been injected at more frequent intervals, it might have made a difference and given a more immediately favorable result. In all, twelve patients were treated by means of the serum, eight males and four females. Their ages ranged from 5 months to 3 years; all but two were under 2 years, and three of these were under 1 year. There were three cases of lobar pneumonia and nine cases of bronchopneumonia. Two patients

died, one of empyema and one of extensive double pneumonia, marasmus and cardiac failure. (Mortality 16.6 per cent.). Two other patients besides those that died were not helped by the serum, but the other eight patients were all more or less improved and in some of the patients the effect of the serum seemed marked. Those patients who received serum early in the disease seemed to be most benefited by its use. This serum should be made in a concentrated form to prevent serum sickness, which has previously been the drawback to the animal serums. The polyvalent, composite serum, while it has not given brilliant results in all cases, is at least an advance in therapeutics in the right direction and apparently in a number of cases limited the disease. To obtain the best results from the serum treatment of pneumonias of mixed infection, the serum should be obtained from horses, not only immunized to the pneumococcus, but also to the other germs which are commonly found to be present in these cases. It is important that in pneumonia the child be injected early in the disease with good sized doses of a concentrated serum. F. C. Z.

Diseases of the Cow in Their Relationship to Human Diseases

(W. G. Savage: Proc. Roy. Soc. Med., March, 1911)

The part which the cow plays as a source of disease in man through the milk supply is studied by Savage under three heads: 1. General systemic disease of the cow without local lesion of the milk organs. 2. General systemic disease of the cow with local lesions in or on the udder and teats. 3. Local affections with little or no general systemic disturbance. Tuberculosis is excluded in this study. The danger from anthrax is a remote one, as the cow usually dies within a few hours after infection, though the bacillus has been recovered from the milk. Widespread outbreaks of food-poisoning have resulted from the consumption of meat infected with the Gaertner bacillus. In cows affected with diarrhea and other symptoms of gastro-enteritis the milk is usually abnormal and decomposes rapidly, and may produce diarrhea. In septic conditions, puerperal septicemia, metritis, etc., the milk is usually markedly altered and no doubt would be prejudicial. Cows are susceptible to Malta fever and the *Micrococcus melitensis* has been found in the milk. Though not mentioned by Savage it also affects goats and is recognized in Malta as the source of Mediterranean fever. In the second group, with local lesions of the teat and udder, are foot and mouth disease and cow-pox, the former of which may be transmitted to man through the milk as attested by a number of cases and outbreaks of the disease. The milkers' hands are likely to be infected with cow-pox, but there is little evidence of the harmfulness of the milk. The most interesting group is the third in which the essential lesions are in connection with the milk-producing organs. They take the form of mastitis and the various conditions described as ulcerated teats. Epidemics of illness ascribed to mastitis have nearly always been of the nature of septic sore throat, although there are one or two in which gastro-enteritis has been the predominant condition, of which Holst records four epidemics in which the organism was the mastitis streptococci. Savage records a large number of outbreaks of this nature extending over a considerable period of time, in some of which several hundred cases were reported. To determine whether the streptococci found in cow mastitis were pathogenic to man Savage conducted some investigations in sixteen cases of human sore throat. Two chief types were found, confirming the results previously found by Andrewes and Horder, the most prevalent type being the variety which they called *Streptococcus anginosus*, while the other was identical with the *S. pyogenes*. Further experiments by Savage led him to the conclusion that the great majority of cases of bovine mastitis are due to an organism not pathogenic to man, but that in certain uncommon cases this condition is caused by a streptococci highly pathogenic to man. The pathogenic and the non-pathogenic types, however, are not clinically distinguishable. If ulcerated teats have

any relationship to human disease Savage believes it may be accounted for in three ways—the ulceration may be part of a general disease of the cow, and through the teat ulcerations the milk may become infected; the teat and udder conditions may be purely local, but due to streptococci or other organisms pathogenic to man; the teat conditions may be due to purely bovine disease, but become secondarily infected by organisms pathogenic to man; in other words, we may have a constitutionally infective cow, a local actively infective cow, and a local passively infective cow. In addition to streptococcic infection, teat lesions may be secondarily infected with diphtheria bacilli, and Savage reports a number of epidemics from this source. As to scarlet fever, Savage believes that the existence of a constitutional disease, bovine scarlet fever, cannot be accepted as proved; but as an explanation of the extensive outbreaks of scarlet fever clearly traceable to milk as at Hendon in 1885 and in certain parts of London and Surrey in 1909, Savage suggests the hypothesis that when the cow is the source of scarlet fever, or other septic disease, it is because it is acting as the carrier of organisms of human origin, often in a purely passive capacity. J. B. C.

Hemorrhagic Disease of the Newborn

(*R. M. Green and J. B. Swift: Boston Med. and Surg. Jour., 1911, clxiv, 454*)

The fifty-one cases which form the basis of this paper occurred in the wards of the Boston Lying-In Hospital from June 19, 1904, to April 1, 1910, a period of nearly six years. The total number of babies born in the hospital during this time was 4,455, showing a percentage incidence of 1.14 per cent. as against 0.57 per cent. in Townsend's series. Of the fifty-one mothers, thirty-one were primiparæ, twenty were multiparæ. In none of the multiparæ of this series is there any record of hemorrhage in previous children. This fact would tend to controvert the theory that the disease is analogous to hemophilia, or in any way dependent on a hereditary dyscrasia. Thirteen of the fifty-one mothers were single, thirty-eight were married. The presentation of the fetus in every case was a vertex. The longest labor of the series ran to seventy hours, but this baby recovered, and of the twenty-five who died, ten were born after less than twelve hours of labor. The average duration of labor for the entire series is fourteen hours thirty-seven minutes, which is only slightly above the general average for a large number of unselected cases. Nine of the labors were forceps deliveries, again about the same percentage as of all cases in the clinic. One of the mothers had pneumonia at the time of delivery, one had mitral regurgitation, and one impending eclampsia. One mother was an epileptic. Three of the puerperia were complicated by slight uterine sepsis, two by mastitis, one by salpingitis, and one by scarlet fever. It does not seem that any of these complications or attendant circumstances could have had any bearing on the hemorrhagic condition. Of the fifty-one cases, thirty-nine occurred during the six months from November to April, inclusive, and only twelve during the six months from May to October, inclusive. This proportion, which is essentially the same as that of the seasonal incidence of such infections as impetigo, diphtheria and bronchopneumonia, the authors think, should confirm the theory of the infectious etiology of the disease, which is more prevalent during the months when ventilation is poorest and general resistance to infection is lowered. Again it is instructive to observe that thirty-three of the cases occurred in distinct groups, after the manner of hospital infections. The average age at onset for the entire series was 3½ days. The average age at onset for the fatal cases was only slightly less, 3 1/5 days. The only two cases that began after the tenth day resulted in recovery. The greatest age at onset among the fatal cases was 9 days, but all the other fatal cases occurred under 7 days. This would seem to indicate that after ten days the disease is infrequent and the prognosis good; that after a week, the prognosis is fairly good; but that under a week the prognosis is poor and the age at onset has no particular bearing on the prognosis. Clinically the cases arrange themselves in

three distinct groups as follows: First, those in which the hemorrhage is principally from the umbilicus; second, those in which it is principally from the mucous or serous membranes; third, those characterized principally by the formation of subcutaneous purpuric patches or ecchymoses. These types the authors designate, respectively, the umbilical, the seromucous and the purpuric, according to which form of hemorrhage predominates. The important bearing of this classification is on prognosis. The mortality of the umbilical type is about 60 per cent., that of the sero-mucous type about 50 per cent., and that of the purpuric type about 22 per cent. The treatment of these patients was supportive, hemostatic and by means of normal rabbit serum, which was given subcutaneously in 30 c.c. doses, repeated two or three times, in case the bleeding recurred after the first dose. The results of treatment are tabulated as follows:

Treatment	Recoveries	Deaths	Total
General Supportive	2	4	6
Local hemostatic	2	5	7
Gelatin	9	4	13
Rabbit serum	12	10	22
None	1	2	3
	26	25	51

Crile's experiments in direct blood transfusion suggested its use in one case, after a dose of rabbit serum had failed to arrest bleeding. The transfusion was successful, but the patient died. F. C. Z.

TUBERCULOSIS AND SYPHILIS

Treatment of Congenital Lues in Infants, by Injecting Salvarsan ("606") Into the Nursing Mother.

(K. Taege: München. med. Wchnschr., 1910, lvii, No. 33; R. Duhot: ibid No. 35; M. Dobrovitz: Wien med. Wchnschr., 1910, No. 38; J. E. R. McDonagh: Brit. Jour. Child. Dis., October, 1910; Meirowsky and Hartmann: Med. Klin., Berlin, 1910, vi, No. 40; P. Ehrlich: Deutsch. med. Wchnschr., 1910, No. 41; J. Peiser: Berl. klin. Wchnschr., 1910, xliii, No. 1.)

Taege was treating a luetic mother in the Freiburg Klinik, and ten days postpartum injected 0.3 gm. of salvarsan into the mother. The infant had shown specific symptoms for two days, and for two days more the symptoms progressed; on the third day a cessation was noticed, and by the fifth there was a complete change for the better. Examination of the mother's milk for arsenic was negative.

In Duhot's case a child in a very serious condition was rescued from almost certain death by the salvarsan treatment ("accidentally") given its mother. The child had no mercurial treatment and was certainly benefited after the injection of the mother. He concludes that a luetic woman treated with salvarsan is the best wet-nurse for a luetic child whose mother can not nurse it.

Dobrovitz had one case, the four months' old child of a mother who denied lues; it showed soon after birth a pustular eruption which gradually spread, and showed other clear signs of lues. The mother showed no clinical signs, but the Wassermann reaction was positive; she was nursing the child, and received one injection of salvarsan. Four days later many of the lesions on the child's skin healed. It is to be noted that in spite of the febrile and other constitutional symptoms exhibited by the mother, for three days after injection the milk secretion was not affected and the child was remarkably quiet.

Meirowsky and Hartmann, instigated by the reports of Taege and Duhot, tried the plan of treating a congenitally luetic infant with the blood-serum of a patient

treated with salvarsan. The mother showed only the typical ulcerated papules on the genitalia, and was delivered of a male child apparently healthy; during the first two weeks it showed no symptoms; then came a typical efflorescence on the palms, soles and buttocks, and later on more symptoms. Since the nursing period of the mother was ended, the child was treated with the blood-serum of a patient treated with salvarsan; two days after the first injection came the first signs of change, the soles of the feet becoming clear; after seven more injections very few symptoms were left, although three days later a coryza and a periostitis of the arm were present. While no complete cure is claimed here, an improvemnt certainly followed, and the authors believe they would have had better results with larger doses of serum.

Peiser tried this treatment in two cases in the clinic of Dr. Ritter in Berlin; the first case had visceral lues, manifest from birth, and evidently fetal; general condition poor, prognosis doubtful. The second patient showed luetic symptoms only a few days after birth, which were confined mostly to skin and mucous membrane; general condition good, prognosis good. The results in both cases were negative, and both infants died; at first all symptoms disappeared, but they soon came again, more severely, and apparently opened the way for a secondary infection. Wassermann reaction was positive in both mothers before the injection of salvarsan; it was absent in the mother of the first case after the death of the infant. The other mother went away before she could be retested.

Ehrlich, in a general discussion of the formation of antibodies after the injection of salvarsan, includes a consideration of the reports of Taege and Duhot, and says that since arsenic was not found at all or at most in minute quantities in the milk of these women treated with salvarsan, and since salvarsan used *per os* even in large doses has but little effect, the possible factor of antibodies must be considered, the sudden death of so many spirochetes having set free a large amount of endotoxins, which went with the milk. This is perhaps analogous to the *säuglings immunität* already described; additional evidence is offered in the fact that the blood-serum of patients treated with salvarsan has a curative effect on new-born luetic children, as reported by Marinesco, Plaut, Scholtz, and L. Michaelis. This latter method is certainly better than the direct one on the child, which may cause severe nutritional disturbances, due probably to the sudden production of endotoxins in the blood, after the sudden dissolution of the spirochetes.

McDonagh refers to the cases of Taege and Duhot, and remarks that if merely injecting the mother is going to cure the child, the latter need not be injected; thereby the risk of poisoning from an overdose is obviated; but one must bear in mind the possibility of a recurrence, if treating the mother is solely relied on, as one can scarcely believe that the amount of antitoxin absorbed from the milk would be as potent as an injection. A. C. Soper, Jr.

Salvarsan Treatment of Infants

(A. Doblin: Berl. klin. Wchnschr., 1911, No. 12)

Doblin treated six infants directly with salvarsan, subcutaneously or intramuscularly. Two were apparently hopeless from the beginning and showed absolutely no improvement. The other four were at the time of the injections in a tolerable condition, and exhibited the varying symptoms of pallor, rhinitis, dermatitis exfoliativa, visceral lues, roseola, or glandular swelling. In contradistinction to the effect on adults, none of these showed a strong necrotic area at the site of the injection, during an observation of over three weeks; only a hard swelling appeared, which neither became red nor ulcerated. On the luetic symptoms the influence was marked, especially on the skin, but least on the rhinitis and glandular swellings. As to the viscera, not enough time elapsed to be certain; of the two cases brought to autopsy, no spirochetes were found in the liver.

No claim is made of an influence for the better as regards the general condition; three months later one patient was still in a very weak condition; one

infant died in a month, of erysipelas; one patient, seen first in a collapse, died one day later; one, very sick, but in no way moribund, died one day later; one child in good condition from the first, still showed adenopathy five weeks later.

No patient, then, could be considered as benefited to any great extent; generally the pallor persisted throughout, and the weight curve did not rise to any extent. A. C. SOPER, JR.

RESPIRATORY SYSTEM

Acute Adenoiditis

(Felix Schleissner: Wien. klin. Wchnschr., 1911, xxiv, 9, p. 310)

Schleissner discusses acute inflammation of the postnasal adenoid tissue in children, which is generally accompanied by cervical adenitis and fever, the cervical adenitis or glandular fever being secondary to the adenoiditis. He considers acute adenoiditis a better name for this condition than glandular fever. The condition is not only found in children of all ages, but even occurs in infants under one year of age. While it is not easy to make the diagnosis on the first day of illness, it is not difficult in a few days, though retropharyngeal abscess may be simulated in young children. Usually every symptom, except the enlarged glands, clears up in a few days. The cause is undoubtedly an infection. The glandular swelling gradually disappears spontaneously. MAURICE OSTHEIMER.

When Shall We Remove Tonsils and What Type of Operation Shall We Do?

(E. A. Crockett: Boston Med. and Surg. Jour., 1911, clxiv, 414)

The author believes that in unskilled hands the operation for removal of tonsils will show a higher mortality than an abdominal section for the removal of the appendix after recovery from an acute attack in the hands of a good surgeon, and therefore it is not wise to advise such removal except for sufficient symptoms. In children one should remove the tonsils (1) in all cases in which the child presents large, non-adherent tonsils, largely filling the cavity of the pharynx; (2) in all cases which are associated with enlarged glands in the neck and in all cases of articular rheumatism in which the tonsil is probably an etiologic factor. These operations should be performed, as a rule, in the quiescent period. Endocarditis, in a more or less chronic state, need not necessarily be regarded as a contra-indication for operation. (3) The tonsils should be enucleated in all cases of repeated peritonsillar abscess. Tonsils should not be removed (1) when they are of moderate size, i. e., projecting not over a quarter of an inch beyond the anterior and posterior pillars; (2) under the promise to the parents that their removal will relieve the child of cold in the head or ear trouble. In adults tonsils which are distinctly pathologic, but which give no symptom at present, though they may have caused trouble in childhood, should not be removed. With this exception indications for operation are the same in adults as in children. The mere fact that a child is under ether for an adenoid operation should not be considered justification for the removal of tonsils.

If the case presents a clear history of infection—peritonsillar abscess, acute articular rheumatism, tubercular infection of the neck—the whole tonsil should be enucleated and removed as completely as possible. This should be done by blunt dissection. In an ordinary case of simple hypertrophy devoid of symptoms, the most common type in children, a perfect result may be obtained by removing enough of the tonsil to bring it down to normal size.

From a consideration of accidents which have followed enucleation of the tonsils, Crockett believes that an operation in the throat requiring the use of general anesthesia is too dangerous a procedure for any one to perform, who is

not thoroughly competent to meet the surgical emergencies which may occur. These comprise ability to ligate the common carotid, to ligate the tonsil pillars, to do an emergency tracheotomy, and to perform artificial respiration.

RICHARD M. SMITH.

BLOOD AND CIRCULATORY SYSTEM

Venous Murmurs at the Root of the Neck in Children

(Carey Coombs: Brit. Jour. Child. Dis., 1911, viii, 109)

In a majority of children varying in age from 3 to 15 years, Coombs heard a murmur immediately below the sternoclavicular joint or joints. It was slightly commoner in boys. It was commoner and louder on the right side. This murmur is continuous, but accentuated at the beginning of systole and of diastole, especially the latter. It is at its loudest during the inspiration. Though often heard with the head in the erect position, it was in such cases heard more clearly, and in some other cases heard only, when the head was fully retracted. Lateral rotation of the head also makes it more clearly audible. It is usually abolished when the patient lies down. It is produced in the internal jugular veins; by what mechanism is not clear to Coombs, though its accentuation by retraction of the head is no doubt due to flattening of the veins against the transverse processes of the cervical spine. Though associated with anemia and febrile states, it is heard also in perfectly healthy children. It is not specially associated with tuberculosis or any enlargement of the intrathoracic lymph-glands, and has no diagnostic value. F. C. ZAPFFE.

Effect of Exercise on Systolic, Diastolic and Pulse Pressures and Pulse Rate.

(O. S. Lowsley: Am. Jour. Physiol., 1911, xxvii, 446)

All types of prolonged exercise which cause an increase in pulse rate cause also a rise in systolic and diastolic pressures. The systolic pressure shows the greater rise, hence there is an increase in pulse pressure which may be interpreted to mean that the heart beats are augmented as well as accelerated. After all types of exercise which were studied, the systolic, diastolic and pulse pressures invariably fall below normal and remain in this subnormal condition for a considerable time. The more exhaustive the nature of the exercise the longer will be the subnormal period which follows. Systolic pressure invariably falls more rapidly than diastolic and hence the pulse pressure becomes weaker. The presence of albumin in the urine coincident with low pressure was observed, just as in the cases reported by Erlanger and Hooker (*Johns Hopkins Hosp. Rep.*, 1904, xii, 145-378). This seems to add another factor to the possible injurious results of long continued exhaustive exercise. The pulse rate, which always increases during exercise, decreases rapidly after its completion. This drop in the curve of the pulse rate is frequently followed by a secondary rise, which is possibly a reflex effect due to the low blood pressure of the subnormal stage. In no case was this secondary rise in pulse rate accompanied by a rise in blood pressure. Vigorous, fatiguing and exhausting exercise is followed by a subnormal blood-pressure, which lasts the longer the more severe the exercise. If the interpretation of these results is correct, the so-called field events, such as shot putting, discus and hammer throwing, jumping, baseball, and exercises of a similar nature are preferable for the rapidly growing youth, to basket ball, football and running races. There is less strain put on the circulatory system by walking a number of miles at a moderate rate than by sprinting 100 yards at top speed. Long distance running and similar forms of exhaustive exercise give rise to serious strain on the heart, as is indicated by the long period of subnormal blood pressure.

FRITZ B. TALBOT.

NERVOUS SYSTEM

The Prevention of Feeble-Mindedness

(E. R. Johnson: Jour. Am. Pub. Health Assn., 1911, i, 90)

From a study of cases in the Training School at Vineland, N. J., the author has compiled statistics of the occurrence of feeble-mindedness in families. In seventy-seven families there were 352 feeble-minded individuals. In the 113 families having relatives in the school, numbering 495, only 177 or 35.8 per cent. were normal. He urges a careful and painstaking collection of statistics to secure the facts on which to base further preventive action. He believes heredity plays a large part in the production of feeble-mindedness, so that the real point of attack is the feeble-minded person who would become a parent. RICHARD M. SMITH.

GENITO-URINARY SYSTEM

Lordotic Albuminuria in School Children

(L. Piesen: Wien. klin. Wchnschr., 1911, xxiv, 1, p. 12)

Piesen has made a series of analyses of urine from school children, both before and after standing five minutes in lordosis; also before and after sitting in the ordinary school position with the arms crossed. In the former he found albumin in from 32 to 46 per cent. of the children; in the latter, in from 12 to 28 per cent. The age of the children was apparently not of any significance; the height of the children, on the other hand, was important, as most of the taller children developed albuminuria. The kidneys were not palpable in four-fifths of the children examined; while albuminuria was found in one-third of these, it also occurred in over half of those in whom the kidneys were palpable. Piesen concludes that the ordinary method of sitting, with the arms crossed, should be forbidden; that the taller the child, the greater is the tendency to lordotic albuminuria; that this disposition increases with age; and, finally, that statistical investigations show that lordotic albuminuria does not depend on movability of the kidneys.

MAURICE OSTHEIMER.

SKIN AND APPENDAGES

Alopecia Epidemic Due to the Microsporon

(R. O. Stein: Wien. klin. Wchnschr., 1911, xxiv, 9, 308)

Stein reports twelve cases of alopecia which he found to be due to the microsporon Audouini. All these cases occurred among the children attending one school in Vienna. The microsporon first attacks the skin situated near the margin of the scalp, as in the nape of the neck, about the ears, etc. Where or how the first child became infected was not discovered.

MAURICE OSTHEIMER.